



## INTRAORBITAL ANEURYSM

A Case of Aneurysm of the Lacrimal Artery

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### SURVEY OF LITERATURE

**A**NEURYSM within the orbit is a rare condition, in spite of the fact that it is commonly referred to in any discussion of the differential diagnosis of exophthalmos and that a number of cases, so diagnosed, have been reported in the literature. In a survey of the literature we have found reports of 68 cases in which a diagnosis of intraorbital aneurysm was made. Very few of these reports contain information concerning any pathologic investigation, and in even fewer do the recorded facts indicate that a true intraorbital aneurysm was present. In the great majority of instances the diagnosis rested on clinical observations alone.

In the early ophthalmologic literature it is evident that the diagnosis of intraorbital aneurysm was usually based (of course, erroneously) on the finding of a pulsating exophthalmos. In 1823 Guthrie<sup>1</sup> made the first diagnosis of orbital aneurysm, basing his diagnosis on autopsy observations. His was the third recorded case of pulsating exophthalmos, being preceded by cases of Travers<sup>2</sup> and Dalrymple,<sup>3</sup> in both of which the diagnosis was "aneurysm by anastomosis." In 1839 Busk<sup>4</sup>

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1. Guthrie, G. J.: *Aneurysms Within the Orbit: Lectures on the Operative Surgery of the Eye*, London, S. Gosnell, 1823, pp. 157-158.

2. Travers, B.: *A Case of Aneurysm by Anastomosis in the Orbit, Cured by Ligation of the Common Carotid Artery*, *Med.-Chir. Tr.*, London 2:1, 1809.

3. Dalrymple, W.: *A Case of Aneurysm by Anastomosis in the Left Orbit*, *Med.-Chir. Tr.*, London 6:111, 1815.

4. Busk, G.: *A Case of Aneurysmal Tumor in the Orbit*, *Med.-Chir. Tr.*, London 22:124, 1839.



reported 2 cases of pulsating exophthalmos and, without supporting pathologic evidence, coined the phrase "true aneurysm in the orbit" as the diagnosis. The greatest impetus was given to this diagnosis by Sir Thomas Nunneley,<sup>5</sup> who in 1859 reported 4 cases of pulsating exophthalmos. He expressed the opinion that "true aneurysm in the orbit" was the cause of the condition in all 4 cases, even after his only autopsy revealed an aneurysm of the internal carotid artery within the carotid sinus. In 1865 Nunneley<sup>5b</sup> described 2 other cases of pulsating exophthalmos, caused in one by an aneurysm of the internal carotid artery and in the other by intracranial extension of a carcinoma of the thyroid gland. In the light of the autopsies in these 2 cases and in the one which he had reported previously, Nunneley revised his earlier opinion and concluded that pulsating exophthalmos is caused by any mass which compresses the ophthalmic vein as it emerges from the orbit. Although in this view he was still in error, he at least had begun to realize that the pathologic process in cases of pulsating exophthalmos usually lies outside the orbit. However, this change in Nunneley's opinion had little effect on the English and American authors, and reports, without pathologic proof, of aneurysm within the orbit continued to appear.

During the same period Baron<sup>6</sup> led a group of French surgeons in gathering data to show that arteriovenous fistula is the commonest cause of pulsating exophthalmos. In 1835 he demonstrated for the first time at autopsy a communication between the internal carotid artery and the cavernous sinus, suggesting the rupture of an aneurysm of the internal carotid artery as the basis of the lesion. His brief report went largely unnoticed, as did that of Henry<sup>7</sup> (Nélaton's case), who in 1855 also found a communication between the internal carotid artery and the cavernous sinus at autopsy in a case in which pulsating exophthalmos developed after the orbit had been pierced by the rib of an umbrella. It required a review by Delens<sup>8</sup> of all the cases of pulsating exophthalmos reported before 1870 to turn the tide of thought toward intracranial arteriovenous fistula as the common cause of pulsat-

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5. Nunneley, T.: (a) Aneurysm of or Within the Orbit: Account of Three Cases, *Med.-Chir. Tr.*, London **42**:165, 1859; (b) Vascular Protrusion of the Eyeball, *ibid.* **48**:15, 1865.

6. Baron: A Case of Ruptured Internal Carotid Aneurysm in the Cavernous Sinus, *Bull. Soc. anat. de Paris* **10**:178, 1835.

7. Henry (interne de l'hôpital): Note sur un aneurysme arterioveneux (communication de carotid interne avec le sinus caverneux) observation dans la service de M. Nélaton, *Bull. Soc. anat. de Paris* **30**:178, 1855.

8. Delens E.: De la communication de la carotid interne et du sinus caverneux (aneuysme arterio-veneux), Paris, Adrien Delahaye, 1870.

ing exophthalmos. His monograph was followed by similar collections of cases by Rivington<sup>9</sup> (1875), Sattler<sup>10</sup> (1880), Dempsey<sup>11</sup> (1886), de Schweinitz and Holloway<sup>12</sup> (1908) and Rhodes<sup>13</sup> (1916), each case strengthening the diagnosis of arteriovenous fistula. Since then, reports of intraorbital aneurysm have been less and less frequent, until, except for a reference by Rand<sup>14</sup> in 1944, the last one, by Vail and Oliver,<sup>15</sup> appeared in 1914. Even in Vail and Oliver's case the diagnosis was presumptive and was not based on actual demonstration of the aneurysm; and in Rand's case available information was inadequate to establish the diagnosis.

In a report by Locke<sup>16</sup> in 1924, who collected 588 cases of pulsating exophthalmos, an arteriovenous fistula within the cranial cavity was discussed almost to the exclusion of aneurysm within the orbit. Intraorbital aneurysm was mentioned only briefly, in the historical note. The same is true of the report published by Martin and Mabon<sup>17</sup> in 1943, on 812 cases of pulsating exophthalmos. Since these two reports, the term "pulsating exophthalmos" has become almost synonymous with a diagnosis of fistula between the internal carotid artery and the cavernous sinus. That trend is almost as erroneous as the old diagnosis of aneurysm within the orbit is shown by Locke's analysis of the 50 autopsies performed in 588 cases which he collected. In 32, or 64 per cent, of these autopsies the pulsating exophthalmos was found to be due to an intracranial arteriovenous fistula, while the remaining 18, or 36 per cent, revealed that intraorbital tumor or simple aneurysm, just posterior to the orbit, caused the condition.

We have found in the literature reports of 6 cases in which the diagnosis of intraorbital aneurysm was based on pathologic changes seen at autopsy or at operation. Few of these reports give satisfactory evi-

9. Rivington, W.: Pulsating Tumor of the Left Orbit, *Med.-Chir. Tr.*, London 58:183, 1875. (Comments are appended with all recorded cases of intraorbital aneurysms.)

10. Sattler, H.: *Pulsirender Exophthalmus*, in Graefe, A., and Saemisch, T.: *Handbuch der gesamten Augenheilkunde*, Leipzig, Wilhelm Engelmann, 1880, vol. p. 745.

11. Dempsey, A.: Case of Orbital Aneurysm, *Brit. M. J.* 2:541, 1886.

12. de Schweinitz, G. E., and Holloway, T. B.: *Pulsating Exophthalmos*, Philadelphia, W. B. Saunders & Company, 1908.

13. Rhodes, G.: Pulsating Exophthalmos, *Ann. Surg.* 63:389, 1916.

14. Rand, C. W.: *The Neurosurgical Patient*, Springfield, Ill., Charles C Thomas, Publisher, 1944, pp. 243-244; personal communication to the authors.

15. Vail, D., and Oliver, J. C.: Aneurysm of the Orbit in an Elderly Woman, Cured by Operation, *Lancet-Clin.* 112:644, 1914.

16. Locke, C. C., Jr.: Intracranial Arteriovenous Aneurysms, Pulsating Exophthalmos, *Ann. Surg.* 80:1-24 and 272-280, 1924.

17. Martin, J. D., Jr., and Mabon, R. F.: Pulsating Exophthalmos, *J. A. M.* 121:330 (Jan. 30) 1943.

dence that the cause of the exophthalmos was simple aneurysm limited to the orbital cavity. To show the reasoning which brought us to this conclusion, the 6 cases will be discussed separately.

CASE 1.—Guthrie's<sup>1</sup> case, reported in 1823, is considered by most authors to be a verified case of intraorbital aneurysm. The entire report of his case, quoted here, will explain the questions which have arisen regarding diagnosis.

I have seen one case of true aneurism of the ophthalmic artery, of both sides, which terminated fatally. The symptoms were similar to those above mentioned, but no tumor could be perceived, the eye was gradually protruded until it seemed exterior to the orbit, but vision was scarcely affected. The hissing noise in the head could be distinctly heard, and was attributed to the aneurism. On death of the patient, an aneurism of the ophthalmic artery was discovered on each side, of about the size of a small nut; the vena ophthalmica-rebralis was greatly enlarged, and obstructed near where it passes through the foramen lacerum orbitalis superius, in the consequence of the great increase in the size the four recti muscles had attained, accompanied by almost cartilaginous hardness, which had been as much concerned in protrusion of the eye as the enlargement of the vessels. The disease existing on both sides prevented an operation on the carotid being attempted, to which indeed the patient would not have submitted.

Delens<sup>8</sup> was the first to question Guthrie's diagnosis, observing that the location of the arterial dilatation, in relation to the bony structures, was not definitely stated. He also expressed the opinion that a more complex lesion than a simple aneurysm was suggested by several statements in the report. Dempsey<sup>11</sup> pointed out that no examination of the cavernous sinus was mentioned. Rivington<sup>9</sup> was not satisfied with the clinical data given. Although the statement that there was an aneurysm on each ophthalmic artery "of about the size of a small nut" seems clear enough, there are other phases of this report which raise some doubts in one's mind: First, bilateral aneurysms of the same size on the same vessels constitute a rare, almost unheard of, coincidence. Second, simple aneurysm practically never produces "hissing" or any other type of noise. The occurrence of such a noise strongly suggests that the patient has an arteriovenous communication. Third, the increase in size of the extraocular muscles and their hardness suggest that the patient may have had a malignant exophthalmos of the type which is sometimes associated with thyroid disease (Naffziger). Lastly, the report is incomplete, and there is no information as to the state of the intracranial vessels, notably the internal carotid artery and the cavernous sinus.

CASE 2.—Carron du Villards<sup>18</sup> in his presentation to the Société anatomique de Paris in 1838, described the case of a woman whom he saw only after her death from a disease of the lower portion of the abdomen. Autopsy revealed an aneurysm of the ophthalmic artery just at the point where the vessel entered the orbit. The author did not state whether the aneurysm was intracranial, intraorbital but did say that it was the size of a small nut. He was unable to obtain any clinical data regarding the affected eye. Delens stated the belief that this case was similar to the one reported in 1861 by Demarquay,<sup>19</sup> in which an aneurysm of the intracranial portion of the internal carotid and ophthalmic

18. Carron du Villards: *Guide pratique pour l'étude et le traitement des maladies des yeux*, Paris, 1838, vol. 1, p. 484.

19. Demarquay: *Traité des tumeurs de l'orbit*, Schmidt's Jahrb. **112**, 1861.

arteries was observed at autopsy. Sattler<sup>10</sup> presented Carron du Villards' case as questionably one of intraorbital aneurysm.

CASE 3.—The lesion in Passavant's<sup>20</sup> case (1866), thought by Sattler to be an intraorbital aneurysm, was diagnosed preoperatively as an aneurysm of the lacrimal artery. The patient, a 9 year old girl, was struck by a knitting needle thrown at her by an angry sister. The needle penetrated the lateral aspect of the lower eyelid. A short time later there developed 6 mm. of exophthalmos and pain in the wounded eye. The condition was thought to be due to an aneurysm of the lacrimal artery because the eye had lost all mobility and was turned strongly inward. Passavant operated, using a lateral approach, similar to the one described later by Krönlein.<sup>21</sup> No dilated vessels were apparent in the lateral portion of the orbit, but Passavant was able to feel a large dilated vessel medial to the optic nerve. He thought that this vessel was the ophthalmic artery but was unable to see or to ligate it. The patient's condition was not improved by his operation. His postoperative conclusion was that the exophthalmos was due to a complex vascular lesion, which he called *l'aneurism diffuse primitif*, a term used in connection with arteriovenous fistula. Certainly, there must be more than a little doubt as to the exact nature of the pathologic anatomy in this case.

CASE 4.—Lewis<sup>22</sup> ligated the dilated ophthalmic artery in a case which he reported in 1907. The patient, a 26 year old man, had been unconscious for an unstated period after a blow on the back of the head. Several weeks after he again became conscious he discovered that his left eye was more prominent than his right. A sensation of "beating" extended throughout his head, increasing in intensity over a period of a year. When Lewis first saw him, there were 6 mm. of proptosis, diplopia, engorgement of the conjunctival and retinal vessels, a bruit and a palpable, pulsating tumor, which could be felt through the upper eyelid. At operation, Lewis used an orbital approach to the lesion. A quotation from his operative report follows:

"The [ophthalmic] artery was found to have curved upon itself, the largest portion having the diameter of a man's little finger. The dissection was long and difficult. The eyeball was everted as far as possible to the temporal side, where the aneurysmal tumor was found to extend backward, gradually reducing in diameter until it wound around the optic nerve near the optic foramen. Several ligatures were placed around the enlarged vessel as the operation proceeded, until at the last with some difficulty the artery was tied off just within the orbital cavity. . . . The interest in this case centers in the fact that, although some portion of the aneurysm extended outside the orbit, a ligature within succeeded in controlling it, and that without removal of the eye."

The situation here, too, is not clear. The facts that the condition developed after trauma, that there was a bruit, that the eye pulsated and that the conjunctival and retinal vessels were engorged all strongly suggested that the man actually had an arteriovenous communication and that the vessel which was gradually

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20. Passavant: *L'aneurism diffuse primitif*, in de Wecker, L.: *Traité théorique et pratique des maladies des yeux*, Paris, Adrien Delahaye, 1866, vol. 1, pp. 733, footnote 2.

21. Krönlein, R. U.: *Zur Pathologie und operativen Behandlung der Dermoid der Orbita*, Beitr. z. klin. Chir., 4:149, 1889.

22. Lewis, F. P.: *Pulsating Exophthalmos, Ligation of the Orbital Artery: Recovery*, Ophth. Rec. 16:66, 1907.

occluded by repeated ligation was a dilated vein receiving arterial blood and pulsating because of the pathologic communication.

CASE 5.—Moutinho<sup>23</sup> reported in 1907 the successful treatment of pulsating exophthalmos by ligation of the common carotid artery. The exophthalmos appeared thirteen years after trauma to the eye had produced a cataract. In 1908 the patient died of pulmonary tuberculosis and multiple multiloculated cerebral abscesses underlying an old fracture of the temporal bone. Moutinho reported the autopsy observation under the title "verificação pela autopsia da cura d'un aneurisma da orbita."<sup>23b</sup> The orbital veins were found to be greatly dilated, but there was no report on the arteries. Immediately beneath the anterior clinoid process on the side corresponding to the pulsating exophthalmos was an aneurysm of the internal carotid artery. It was the size of an almond, round, very hard and filled with an organized clot. Although it was within the cavernous sinus, no point of communication could be found between the artery and the vein. No mention was made of an aneurysm within the orbit. It is obvious that this case was one of a primary intracranial rather than of an intraorbital lesion.

CASE 6.—In Dempsey's<sup>11</sup> case there was undoubtedly an intraorbital vascular anomaly, but this was only part of an extensive malformation of the internal carotid artery. In addition to a sacculated aneurysm, the size of a "mandarin orange," within the orbit, there were an abscess of the middle cranial fossa and an aneurysm of the internal carotid artery extending from the entrance of the vessel into the cranial cavity to the origin of the ophthalmic artery. The ophthalmic artery was dilated to four times its usual size up to the point of its entrance into the orbit. The entire circle of Willis was dilated, as was the petrosal sinus on the opposite side. The ophthalmic artery on the opposite side was of normal size. No arteriovenous fistula could be found in this case.

Rand<sup>14</sup> briefly noted a case of aneurysm of the ophthalmic artery. The patient complained frequently of pain behind the left eye, accompanied with a noise in her head and a premonition of death. A few minutes after she had experienced excruciating pain, her left eyeball was observed to bulge, and she died shortly thereafter of a ruptured aneurysm. The report of the autopsy, with which Dr. Rand has supplied us, does not provide sufficient information to permit of a definite diagnosis.

Other cases have been referred to as instances of verified intraorbital aneurysm by authors collecting cases of pulsating exophthalmos. When the original articles reporting these cases are consulted, it is obvious that the pathologic findings do not support the diagnosis. Locke made the statement:

When in 1839, Busk confirmed Guthrie's findings by autopsy of another case, it soon became accepted, at least in England, that aneurysms of the ophthalmic artery were the cause of this clinical complex.

This statement was repeated by Martin and Mabon,<sup>17</sup> using "Burke" instead of "Busk." In his paper, Busk reported 2 cases of pulsating

23. Moutinho, M.: (a) Aneurisma da orbita esquerda, *Med. contemp.* **25**: 90-93, 1907; (b) Verificação pela autopsia da cura d'un aneurisma da orbita, *ibid.* **26**:34-36, 1908.

exophthalmos, in both of which ligation of the carotid artery resulted in cure. In each case Busk made the diagnosis of intraorbital aneurysm, but neither patient died while under his care, so that no autopsy was performed. Sattler expressed the opinion that both Busk's patients had arteriovenous fistula; with this we would agree.

Lansdown<sup>24</sup> and Terry and Fred<sup>25</sup> each reported a case of fistula between the nasal artery and the ophthalmic vein. In both these cases a pulsating mass presented in the inner canthus of the eye and the lesion was cured by the local ligation of the feeding vessels. These cases probably represent arteriovenous fistula within the orbit.

It is obvious from this review of the literature that, although the diagnosis of intraorbital aneurysm has been made frequently, it has rarely been confirmed. In the vast majority of instances in which such a diagnosis was made as a causative factor in pulsating exophthalmos, a review of the case would point to an arteriovenous fistula as the most likely cause of the disturbance.

In the case to be presented an intraorbital aneurysm was found at operation and removed. The severe, nonpulsating exophthalmos, with paralysis of the extraocular muscles, was completely relieved.

#### REPORT OF CASE

*Nonpulsating exophthalmos of the left eye, of two months' duration.*

*Examination:* Severe proptosis of the left eye; distention of the periorbital, conjunctival and retinal vessels; paralysis of ocular movements; blurring of optic disk; visual acuity, 20/20 (right eye) and 20/70 (left eye); ptosis of left upper eyelid; pupil small and sluggish.

*Operation:* Transcranial exploration of orbit and removal of aneurysm of lacrimal artery. Complete recovery.

A. M., a white woman aged 58, single, a housekeeper, gave a history of congestion of the left eye, which had appeared three weeks before, and of soreness of the eye, starting four or five days prior to her first office visit to one of us (H. M.), in December 1946. Edema of the bulbar conjunctiva with mild congestion was present in the lower half of the globe. Visual acuity was 20/40 in the affected eye. The nerve head and the vascular ratio were regarded as normal. The intraocular pressure was increased, measuring 37 mm. (Schiøtz). Five days later proptosis was noted. The conjunctival vessels were tortuous. At the same time the retinal veins were beginning to show distention. The visual field for the affected eye showed slight concentric constriction. Roentgenographic studies of the orbits and paranasal sinuses revealed a normal condition. On Jan. 17, 1947, proptosis was pronounced, and there was limitation in motion down and to the left and up and to the right. The patient was hospitalized and seen in consultation

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24. Lansdown, F. P.: A Case of Varicose Aneurysm of the Left Orbit, Brit. M. J. **1**:736, 1875.

25. Terry, T. L., and Fred, G. B.: Abnormal Arteriovenous Communication in the Orbit, Involving the Angular Vein, Arch. Ophth. **19**:90 (Jan.) 1938.

with Dr. Peter C. Kronfeld, who stated that orbital venous thrombosis should be ruled out. After a week of treatment with heparin, there was no change in the condition of the eye, and it was concluded that the space-occupying lesion in the orbit was either an aneurysm or an hemangioma; and a transcranial exploration of the orbit was thought advisable. The intraocular pressure was consistently elevated; the veins in the retina had become greatly distended, and large, flame-shaped hemorrhages had developed in all four quadrants of the fundus. The exophthalmometric reading (Luedde) measured 10 mm. in the right eye and 18 to 19 mm. in the left eye. The patient was admitted to the Chicago Memorial Hospital on February 27 for exploration.

The past history was noncontributory, except for the statement that the patient had been treated for bilateral tinnitus for about one year before the onset of the exophthalmos. The tinnitus had diminished with treatment but had not disappeared.

The family history did not reveal any case of an orbital lesion.

*Physical Examination.*—On her admission to the Chicago Memorial Hospital (February 27), the patient was well developed and well nourished. She did not appear ill. There was a small palpable lymph node in the left side of the neck. The breasts, heart, lungs and abdomen were normal. The blood pressure was 120 systolic and 80 diastolic; the pulse rate was 68 per minute.

The left eye protruded. The periorbital skin was edematous and reddened. The conjunctiva was chemotic and intensely injected. There were pronounced ptosis of the left upper eyelid and severe limitation of the ocular movements laterally, medially and upward. The left pupil was smaller than the right and reacted sluggishly to light and in accommodation. There were slight blurring of the margins of the left optic disk and severe engorgement of the retinal vessels in the left eye. The peripheral visual fields were full, and the uncorrected visual acuity was 20/20 in the right eye and 20/70 in the left eye. The corneal reflex was present and normal bilaterally. In spite of the complaint of tinnitus, hearing was normal. The right eye was unaffected in any way.

*Laboratory Examination.*—The urine was normal. There were 4,450,000 red blood cells, 83 per cent hemoglobin and 7,250 white blood cells, with 66 per cent neutrophils. The Wassermann and Kahn tests on the blood gave negative reactions.

*Roentgenologic Examination.*—There were no demonstrable lesions in the orbits. Studies of the chest and the paranasal sinuses showed nothing abnormal.

*Preoperative Impression.*—The proptosis was thought to be due to an intra-orbital mass, probably vascular.

*Operation* (February 28).—A coronal incision was made just posterior to the hair line, and a frontal osteoplastic flap was reflected on the left side. The dura mater was firmly adherent to the inner table of the vault of the skull, owing to the presence of hyperostosis interna frontalis. The frontal lobe was elevated extradurally to expose the roof of the orbit. The roof of the left orbit was removed; anteriorly to the vertical portion of the frontal bone, laterally to the lateral margin of the orbit medially to the ethmoid cells and posteriorly to the sphenoid ridge and the optic foramen. On palpation through the orbital capsule, a firm mass running anteroposteriorly behind the bulb in the lateral portion of the orbit could be felt. When the orbital capsule was opened, the fat protruded under considerable tension. The levator palpebrae superioris and

superior rectus muscles were dissected from the fat and retracted medially. Lying lateral and slightly inferior to these muscles, a grayish blue cylindric mass was discovered (fig. 1). This mass was about the diameter of a lead pencil

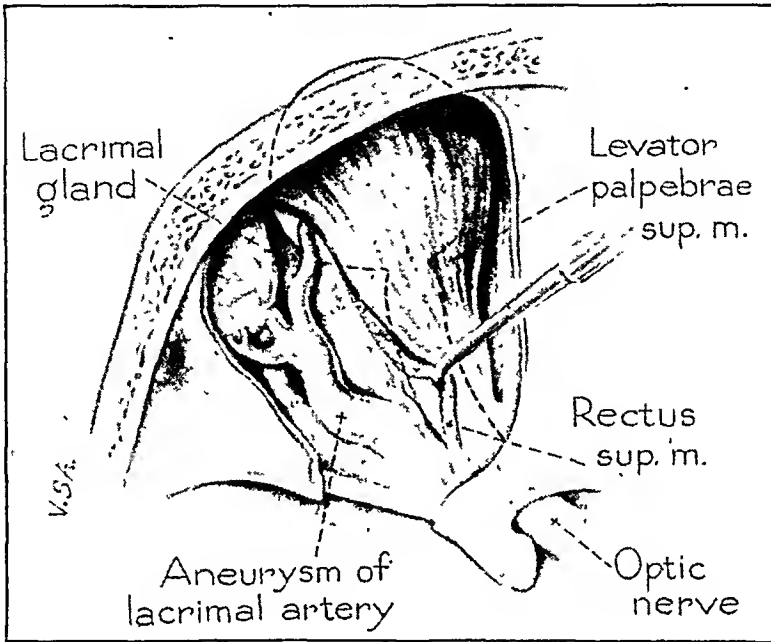


Fig. 1.—Artist's elaboration of the surgeon's sketch made immediately after the operation. The roof of the orbit has been removed. The aneurysm of the lacrimal artery is seen lying in the posterolateral part of the orbit.



Fig. 2.—The aneurysm in cross section. Hematoxylin-eosin stain;  $\times 16$ .

and was 2 cm. in length. It pulsated synchronously with the heart beat. Anteriorly, it divided into three branches. The largest of these curved medially, and its



destination could not be accurately determined. The two lateral branches were smaller and entered the lacrimal gland. All three branches were divided between silver clips, and the anterior portion of the aneurysm was lifted from its bed. The posterior end of the lesion was in the region of the superior orbital fissure, the roof of which was removed to determine the relation of the vessels. The posterior end of the aneurysm was sectioned between a series of silver clips. The dura mater over the floor of the anterior cranial fossa was incised, exposing the orbital surface of the frontal lobe, the sylvian vessels and the tip of the temporal lobe



Fig. 3—The aneurysmal wall. The circular muscle fibers of the media are widely separated by edematous tissue. The longitudinal bundles of muscle fibers at the periphery are more compact. There is no layer of elastic tissue. Hematoxylin-eosin stain,  $\times 80$

Medially, both anterior clinoid processes and the optic nerves were clearly seen. The intracranial vessels were of normal size and relation. No vascular dilatation or other abnormality was seen. The orbital capsule was left open; the frontal lobe was returned to the anterior cranial fossa, and the bone flap was replaced and secured with sutures.

*Pathologic Report.*—The specimen consisted of a blood vessel 2 cm. in length and 4 mm. in diameter (fig. 2). Microscopically, the aneurysm had a distinctly

abnormal wall. The media was very much thickened and its muscle was myx-edematous (fig. 3). The elastic layer was not present.

*Postoperative Diagnosis.*—The diagnosis was aneurysm of the left lacrimal artery, contained entirely within the orbit.

*Postoperative Course.*—Mental aberrations appeared on the fifth postoperative day. These "frontal lobe signs" persisted for three or four days and then subsided completely. At the patient's discharge on March 13, her speech and memory were normal. There was postoperative increase in periorbital edema, but this was subsiding rapidly when she left the hospital. There was moderate ptosis of the left upper eyelid at that time.

On March 27, the patient was feeling very well. At that time, the left pupil reacted sluggishly; there was pulsation of the retinal arteries in the left eye synchronous with the pulse, and many superficial hemorrhages appeared along the course of the veins in all quadrants. The intraocular pressure measured 26 mm. (Schiotz), being normal for the first time since the proptosis had been noted, prior to operation. The exophthalmometric reading was 10 mm. in the right eye and 13 mm. in the left eye.

On April 30, corrected visual acuity was 20/20 in the left eye. There was slight exophthalmos. Ocular motility was normal, as was the intraocular pressure. The retinal hemorrhages were no longer visible.

On July 8, the patient still noticed slight exophthalmos, but only when she became tired. There was no complaint regarding vision, and the ocular movements were unimpaired.

In December 1947, the peripheral fields on the left still showed 5 to 15 degrees of concentric constriction. The intraocular pressure and the ratio of the retinal vessels were normal.

On Jan. 7, 1948, there was no complaint referable to the left eye. The patient commented, however, that the eye pulsed occasionally, especially when she became tired. The tinnitus had disappeared. There was slight enophthalmos. The ocular movements were full. The retinal vessels and the optic disks were normal. The uncorrected visual acuity was 20/40 in the left eye and 20/30 in the right eye. The peripheral fields still showed concentric constriction on the left. Roentgenographic examination of the orbit revealed the silver clips which occluded the arterial communications of the aneurysm, and the defect in the bone, but no other abnormality.

#### COMMENT

A tabulation of signs and symptoms which would lead to a differentiation of intraorbital aneurysm and intracranial arteriovenous fistula cannot be made from the small number of cases, many of them questionable, of intraorbital aneurysm which have been reported up to the present time. Intraorbital aneurysm is certainly a rare condition. The reasons for this rarity pointed out by Nunneley<sup>5b</sup> in 1865 are still plausible: Arteries anywhere in the body of the caliber present in the orbit infrequently form aneurysms; and, in order to produce clinical manifestations, an aneurysm of the orbit would of necessity be relatively large, so as sufficiently to compress the areolar tissue which fills the

orbital cavity. Nunneley was aware that a small mass just posterior to the orbit could produce exophthalmos by compromising the venous blood flow, but he made no mention of similar conditions occurring just within the orbit.

The origin of the aneurysm in the case reported here is not clear, but the lack of elastic tissue in the arterial wall suggests a condition similar to that in the congenital aneurysms of the intracranial vessels. The development of the first symptoms during the sixth decade of life is unusual in the case of a congenital lesion, but it is not unheard of with intracranial aneurysms. The lacrimal artery most frequently arises from the ophthalmic artery soon after it enters the orbital cavity. It may, however, arise from the intracranial portion of the ophthalmic artery, from the middle meningeal artery or, more rarely, by a large anastomosis between the lacrimal branch of the middle meningeal artery and a recurrent branch of the ophthalmic artery. In these instances the lacrimal artery enters the orbit through the superior orbital fissure.<sup>26</sup>

The chemosis and injection of the conjunctiva, the distention of the retinal veins and the retinal hemorrhages are all evidence of venous obstruction. This interference with the venous drainage of the orbit was probably directly responsible for the exophthalmos, the impaired vision and the increased intraocular tension. Whether it resulted from mere compression of the veins, or from a venous thrombosis, as Dr. Kronfeld originally postulated, can now be only a matter for speculation.

As demonstrated by the experience of Passavant and Lewis, the orbital approach to vascular lesions of the orbit is dangerous and liable to failure. With the transcranial route advocated by Naffziger<sup>27</sup> and Dandy,<sup>28</sup> the entire lesion, both intracranial and intraorbital, can be visualized, with little danger to the eye or to the optic nerve.

As this review of the literature has clearly shown, exophthalmos is so frequently associated with intracranial disease, rather than with a lesion limited to the orbit, as to make the ability to explore the intracranial cavity a valuable addition to the operative procedure. Furthermore, the extent of the exposure by the transcranial route, the much better visualization of both intraorbital and intracranial structures and the greater ease and safety in controlling the blood supply make this the preferable surgical approach in many cases.

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26. Jackson, C. M.: *Morris' Human Anatomy*, ed. 9, Philadelphia, P. Blakiston's Son & Co., 1933.

27. Naffziger, H. C., and Jones, O. W.: *The Surgical Treatment of Exophthalmos Following Thyroidectomy*, J. A. M. A. **99**:638 (Aug. 20) 1932.

28. Dandy, W. E.: *Orbital Tumors*, New York, Oskar Piess, 1941; *Results Following the Transcranial Operative Attack on Orbital Tumors*, Arch. Ophth. **25**:191 (Feb.) 1941.

## SUMMARY

A case of exophthalmos due to aneurysm of the lacrimal artery contained entirely within the orbit is reported. The lesion was removed by the transcranial route, and the patient is entirely well, over a year after operation, with normal vision and normal ocular movements in the affected eye.

A survey of the literature on orbital aneurysm revealed no other verified case of aneurysm of the lacrimal artery. Reports of 6 cases in which an intraorbital aneurysm was said to have been visualized either at operation or at autopsy are reviewed, but in none is the diagnosis without question. Because of this lack of verified cases, no criteria can be set up on which a differential diagnosis of an aneurysm within the orbit may be based. The case presented here is evidence that orbital aneurysm can be manifest clinically by unilateral exophthalmos without pulsation, but with evidence of venous obstruction, increased intraocular tension and failing vision.

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## VISUAL ACUITY WHILE ONE IS VIEWING A MOVING OBJECT

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FOVEAL visual acuity while one is viewing a moving object has received curiously little attention. In fact, the only reference to this subject which I have been able to find is a note by Langmuir<sup>1</sup> in which, in an effort to estimate the speed of a deer botfly, he whirled above his head a piece of solder fastened to a string and noted at what speed the piece of solder appeared blurred. I have discussed this problem.<sup>2</sup>

There have been investigations of the minimum velocity perceptible as movement<sup>3</sup> and the way in which this minimum velocity varies from center to periphery of the visual field.<sup>4</sup> There have also been investigations of the minimum length of path which permits motion to be perceptible.<sup>5</sup> Some have claimed<sup>6</sup> that there is "visual anesthesia" while the eyes are voluntarily moving. Bethe's "Handbuch,"<sup>7</sup> Duke-Elder,<sup>8</sup> Troland<sup>9</sup> and Vernon<sup>10</sup> make no mention of any determination of visual acuity while the eye is following a moving object.

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This investigation was supported in part by a grant from the American Optical Company.

From the Howe Laboratory of Ophthalmology and the Massachusetts Eye and Ear Infirmary.

1. Langmuir, I.: The Speed of the Deer Fly, *Science* **87**:233 (March) 1938.
2. Ludvigh, E. J.: Visibility of the Deer Fly in Flight, *Science* **105**:176 (Feb.) 1947.
3. Munck, G. W.: Gesicht und Sehen, in *Physik. Wörterbuch* **4**:1457, 1828.
4. Bourdon, B.: La perception visuelle de l'espace, Paris, Lille, 1902, p. 201.
5. Basler, A.: Ueber das Sehen von Bewegungen, *Arch. f. d. ges. Physiol.* **115**:582-601, 1906.
6. Holt, E. B.: Eye-Movement and Central Anaesthesia, *Psychol. Rev. Monog. Supp.* **4**:3-45, 1903. Dodge, R.: Visual Perception During Eye-Movement, *Psychol. Rev.* **7**:454-455, 1900.
7. Bethe, A.; von Bergmann, G.; Emden, G., and Ellinger, A.: *Handbuch der normalen und pathologischen Physiologie*, Berlin, Julius Springer, 1931, vol. 12, p. 2.
8. Duke-Elder, W. S.: *Text-Book of Ophthalmology*, St. Louis, C. V. Mosby Company, 1932, vol. 1.
9. Troland, L. T.: *The Principles of Psychophysiology*, New York, D. Van Nostrand Company, Inc., 1929, vol. 1.
10. Vernon, M. D.: *Visual Perception*, London, Cambridge University Press, 1937.

In view of the absence of any information on this subject, it was thought advisable to conduct an investigation of the problem, particularly since the eyes are so often and critically employed under these conditions.

#### PRESENT INVESTIGATION

The simplest type of motion first to be investigated seemed to be simple rotary motion of the test object. This was produced by inserting prisms of various strengths in a ball bearing and then driving the ball bearing by means of a variable speed drive. The result was that the object viewed appeared to travel about in a circle in a plane perpendicular to the line of sight. Monocular observation was used. The test objects employed were Snellen letters. Eight letters were selected from various charts so that the same eight letters could be used on the 20/100, 20/70, 20/50, 20/40, 20/30, 20/20, 20/15 and 20/10 lines. The maximum distance of observation conveniently available was 5 meters. When the prism was rotated rapidly enough to decrease vision below 20/100, the 3 observers were moved up to a distance of 2 meters from the test object.

TABLE 1.—*Relation of Visual Acuity to Increasing Angular Velocity of the Test Object*

Angular Velocity of Letter Presented (Degrec/Sec.)	Visual Acuity Expressed as a Fraction of the Acuity at 0°/Sec. Angular Velocity	
	4Δ	12Δ
0.....	1.000	1.000
12.....	0.887	0.886
25.....	0.538	0.806
38.....	0.204	0.675
50.4.....	0.103	0.621
61.5.....	0.083	0.456
75.6.....	.....	0.299

The experimental procedure was as follows: With the prism rotating at a given speed, the lowest line was determined which resulted in ten successive correct readings of the Snellen letters. The Snellen letters were presented in an order previously determined by the chance selection of cards. On the next lowest line, say the 20/20 line, suppose that seven of the ten letters were correctly read, one would reason, somewhat arbitrarily, that when three errors were made, had the letters been of 20/30 size, they would have been correctly read, since the subject had just previously read ten letters correctly on this 20/30 line. We concluded that on the ten occasions just tested, the subject exhibited 20/20 vision on seven occasions and 20/30 vision on three occasions and that the acuity was therefore intermediate between these two values; more specifically, that it was 20/22.2.

When the apparent motion of the letter is in a circle in a plane perpendicular to the line of sight, it is not immediately apparent what one should characterize the angular velocity of the letter. However, the simplest way of thinking about the matter would seem to be this: Suppose that the apparent movement of the letter is such that it travels around the circle, say five times per minute. Furthermore, suppose that the circumference of this circle is 10 cm. and that the distance of observation is 5 meters; then the letter is traveling 50 cm. per minute. If it were traveling not in a circle in a plane perpendicular to the line of view but, rather,

in a circle around the subject's head at a distance of 5 meters and at a speed of 50 cm. per minute, then it would be going around the subject's head at 5.73 degrees per minute; and it is in this fashion that the angular velocity of the object is defined when the rotating prism is employed.

Figure 1 shows the manner in which visual acuity deteriorates with increasing angular velocity of the test object, and the data are presented in table 1.

It will be observed that when a prism of  $4\Delta$  is being rotated at a speed sufficient to cause an angular velocity of 62 degrees per second

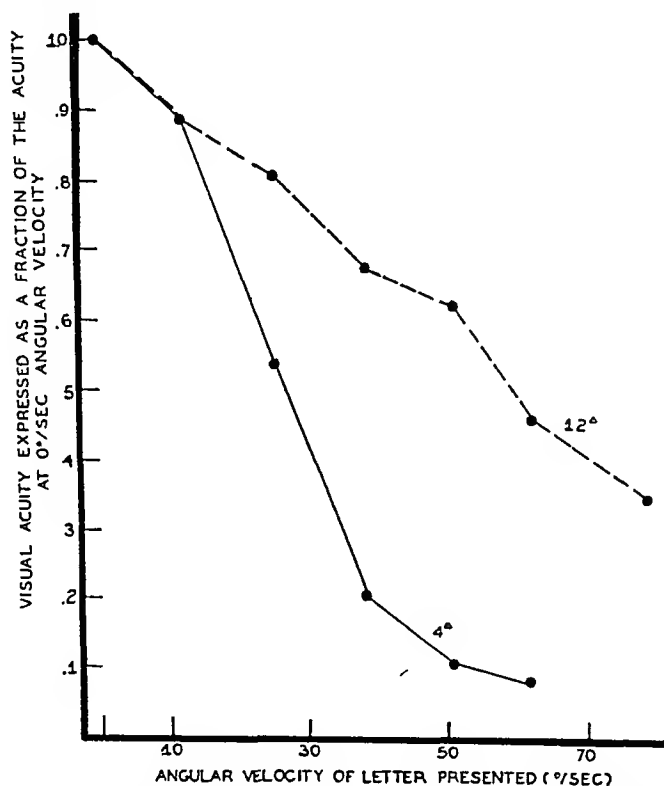


Fig. 1.—Deterioration of visual acuity with increasing angular velocity of the test object.

the visual acuity has been reduced from 20/20 to below 20/200 degrees. Also, in the figure are shown the results obtained with a  $12\Delta$  prism. It will be observed that when an angular velocity of 62 degrees per second is produced by the use of a  $12\Delta$  prism, vision is reduced to about 20/40. This means that when the large prism is employed, the same angular velocity of the letter produces much less deterioration of visual acuity than when the small prism is used. If one may greatly oversimplify the situation, in making a full rotation, innervation of the muscles occurs in the following order: first, the superior rectus muscle, then some of the internal rectus, then the internal rectus alone, then

some of the inferior rectus, and so on, with accompanying inhibitions of the antagonistic muscles. It may be, then, that the falling off of acuity while the eye is following an object moving in a circular path is attributable to inability to repeat the necessary cycle of innervation more than so many times per minute, and it appears, indeed, that this lack of ability to change innervation sufficiently rapidly is a cause of the deteriorating visual acuity with increased speed of motion of the test object. But that this is not the sole factor is shown by the experimental

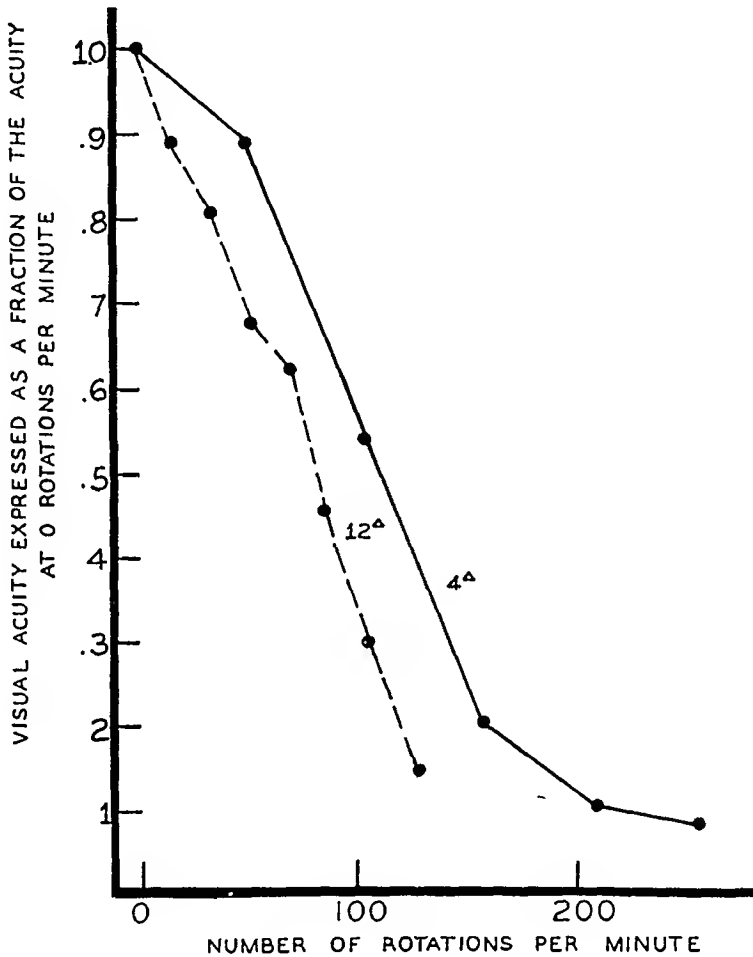


Fig. 2.—Relation of visual acuity to number of rotations per minute of the test object.

data presented in table 2 and shown graphically in figure 2. Here plotted on the horizontal axis is not the angular velocity of the letter in degrees per second, but the number of rotations of the letter per minute. Consider the point at which the number of rotations per minute is slightly in excess of 100. With the 4 Δ prism, the acuity is better than 20/40, while with the 12 Δ prism the acuity is 0.3, or about 20/70; yet the eye need make no greater number of rotations for the 12 Δ prism than for the 4 Δ prism, so that the percentage rate of change of innervation cannot here be the controlling factor. However, with the



12  $\Delta$  prism, the eye must travel through a considerably greater distance, and therefore at a higher angular speed. This indicates that the higher the angular velocity of the test letter, the more the acuity will be reduced. We conclude that when the eye follows an object moving about in a circle in a plane perpendicular to the line of sight, the acuity will be reduced by reason either of the inability of the eye to move sufficiently rapidly or of the inability of the subject to adjust the relative innervation to the various ocular muscles sufficiently rapidly or of both.

The question arises: What is the cause of the reduction of acuity when the eye is following a moving object? Perhaps the first hypothesis to be considered is that acuity decreases when the object is moving

TABLE 2.—*Relation of Visual Acuity to Number of Rotations per Minute of the Test Object*

Visual Acuity	Number of Rotations per Minute	Visual Acuity Expressed as a Fraction of the Acuity at 0 Rotations per Minute
4 $\Delta$ .....	0	1.000
	50	0.887
	104	0.538
	158	0.204
	210	0.103
	256	0.083
12 $\Delta$ .....	0	1.000
	16.6	0.886
	34.6	0.806
	52.6	0.675
	70.0	0.621
	85.3	0.456
	105	0.299
	123	0.147

because imperfect pursuit movements of the eye result in extrafoveal portions of the retina being utilized. An examination of the data shows that this hypothesis can account for only a negligible fraction of the loss of acuity experimentally observed. Consider the instance in which the 4  $\Delta$  prism is being rotated. Suppose that pursuit movements of the eye were completely ineffective and that the eye merely fixated the center of the circle, which is the path in which the Snellen letter is moving. Then, under these conditions, the letter would be only 2 degrees from the fovea. Figure 3 shows some of the results of my investigation of extrafoveal visual acuity as measured with Snellen test letters,<sup>11</sup> and the data are given in table 3. It may be seen that at 2 degrees from the fovea visual acuity has deteriorated only to about 0.8, or 20/25.

11. Ludvigh, E. J.: Extra-Foveal Visual Acuity as Measured with Snellen Test-Letters, *Am. J. Ophth.* 24:303, 1941.

This is clearly insufficient by a factor of 5 to account for the loss of acuity produced by rotating the 4  $\Delta$  prism. Therefore, when the eye is following a moving object, the extrafoveal position of the image is a negligible factor in the observed reduction of acuity.

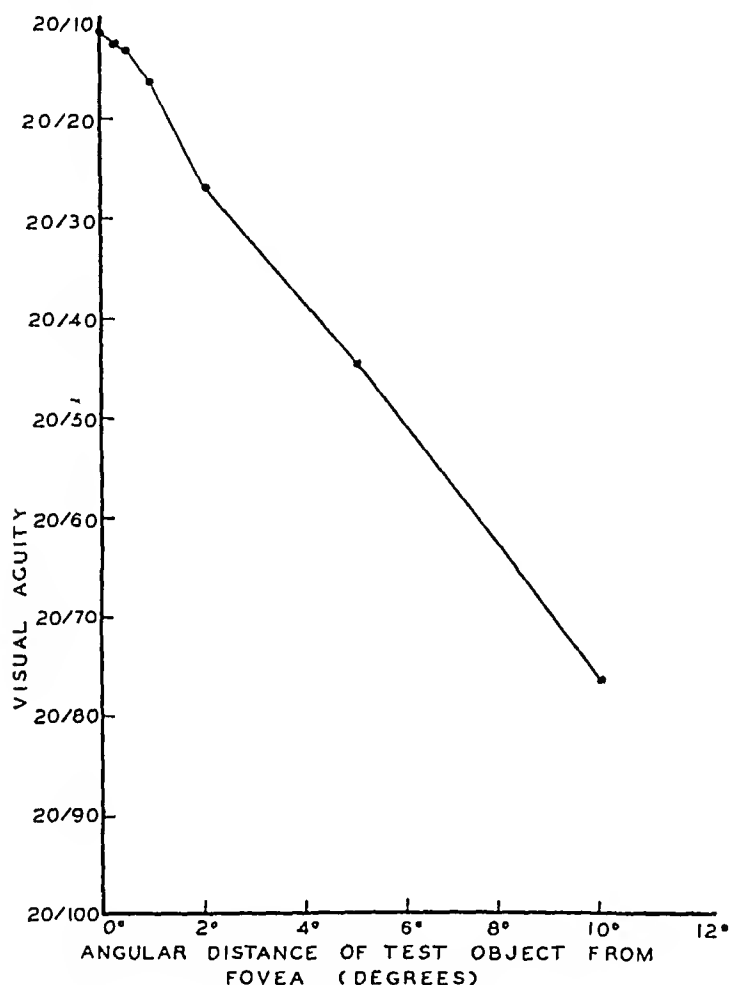


Fig. 3.—Relation of visual acuity to angular distance of the test object from the fovea.

TABLE 3.—*Relation of Extrafoveal Visual Acuity to Angular Distance of Test Object from Fovea*

Angular Distance of Test Object from Fovea (Degrees)	Visual Acuity
0	20/11.65
0.25	20/12.58
0.50	20/13.21
1.0	20/16.81
2.0	20/27.36
5.0	20/45.03
10.0	20/76.80

Another hypothesis is that imperfect pursuit movements of the eye, although maintaining the image in the immediate vicinity of the fovea, nevertheless result in a motion of the image on the retina which reduces

visual acuity. The eye is unable to match the exact rate of movement of the object, and hence the image is continually moving over the retina as the eye goes ahead of, and lags behind, the moving object.

If this hypothesis is correct, it is motion of the image on the retina which produces the deterioration of visual acuity. This motion would result in any given portion of the retina receiving less intensity contrast than it would if the eye and object were stationary. It might, therefore,

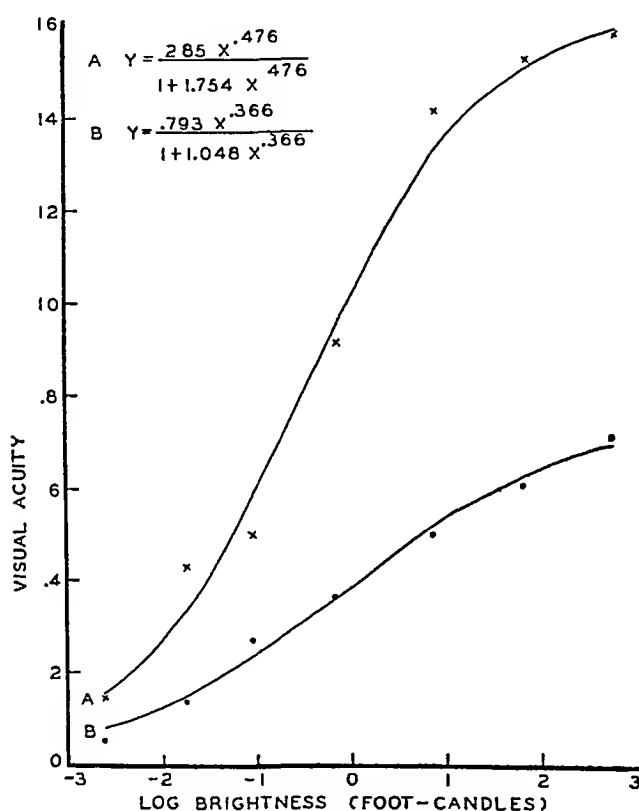


Fig. 4.—Relation of the visual acuity to intensity of illumination.

TABLE 4.—Relation of Visual Acuity to Intensities of Illumination

Log Brightness (Foot Candles)	Visual Acuity, Rotations/Min.	
	0	90
2.703	1.57	0.709
1.772	1.52	0.607
0.837	1.41	0.500
-0.197	0.916	0.360
-1.051	0.500	0.269
-1.764	0.428	0.132
-2.616	0.142	0.0427

be thought that high intensities of illumination would particularly aid visual acuity when the eye was moving. Figure 4 and the data in table 4 show that when the image is moving on the retina high intensities may

advantageously be employed. The test objects used in obtaining these data were Landolt rings. The brightly illuminated area subtended about 5 degrees at the eye, and for these conditions the characteristic sigmoid curve relating visual acuity and log intensity was found. It may be noted that the highest intensities of illumination produce little improvement in acuity when the object is stationary. This is indicated by the flattening out of the upper curve of the graph at high illuminations. The lower curve of the graph shows the results obtained when the test object is being displaced by a rotary prism at a velocity in path of 90 degrees per second. Here, even at the highest intensity of illumination available, about 505 foot candles, acuity is still improving. This suggests that, although for ordinary purposes about 10 foot candles is adequate illumination, an illumination of 1,000 foot candles might be advisable when the eye is following a rapidly moving object.

Since it is difficult visually to extrapolate a curve from the observed experimental points, the data were fitted by the method of least squares to the empiric function  $y = \frac{ax^c}{1 + bx^c}$ , where  $y$  is visual acuity and  $x$  is the illumination in foot candles on the chart. The use of the function  $y = \frac{ax^c}{1 + bx^c}$  implies that visual acuity will become zero when the illumination is zero, and also that as the illumination becomes great visual acuity will approach  $\frac{a}{b}$  in value. No assumption is made as to nature of the process, photochemical or other, mediating the relation of brightness to visual acuity.

When the object is stationary, the data fitted by the method of least squares give rise to the curve  $y = \frac{2.85 x^{0.476}}{1 + 1.75 x^{0.476}}$ . The maximum value of visual acuity predicted by this formula is then  $\frac{2.85}{1.75}$ , or 1.62. Ninety per cent of this final value of visual acuity is 1.46, and this visual acuity is attained when the illumination is 30 foot candles. When the object is moving, the data fitted by the method of least squares give rise to the curve  $y = \frac{0.793 x^{0.306}}{1 + 1.05 x^{0.306}}$ . The maximum value of visual acuity predicted is 0.757, and 90 per cent of this value is not achieved until the intensity of illumination reaches 360 foot candles. It thus appears that a quantitative analysis of the data confirms the notion that high intensities of illumination might be advisable in following a moving object. This problem is being further investigated at still higher intensities of illumination.

#### SUMMARY

Visual acuity was determined while the test object viewed appeared to move in a circle in a plane perpendicular to the line of sight. The diameter of the circle and the velocity of the test object were varied. It is shown that when the eye is following such a moving object, acuity

is reduced by reason either of the inability of the eye to move sufficiently rapidly or of the inability of the subject to adjust the relative innervation to the various ocular muscles sufficiently rapidly or of both. It is shown that in following a moving object the extrafoveal position of the image is a negligible factor in producing the observed reduction of acuity.

The hypothesis is that imperfect pursuit movements, although maintaining the image in the immediate vicinity of the fovea, nevertheless result in a motion of the image on the retina which reduces visual acuity. This motion would result in the retina's receiving less intensity contrast than it would if the eye and object were stationary. The hypothesis tends to be confirmed by observations showing that when the test object is moving, high intensities of illumination may advantageously be employed to increase visual acuity.

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# MECHANICS OF INTRACAPSULAR CATARACT EXTRACTION

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THERE can be little controversy among modern ophthalmic surgeons regarding the advantages and desirability of the intracapsular method of cataract extraction.

As Arnold Knapp<sup>1</sup> has pointed out in his classic paper:

The amount of literature that has arisen on the subject of the intracapsular extraction is bewildering, but some general direction can be recognized. The trend seems to be in favor of an operation in which a firm hold is taken of the capsule with the forceps without tearing it, concentrating the traction to one area and with a hook or similar instrument exerting pressure externally at the lower corneal margin, in order to raise vitreous pressure and to rupture the suspensory ligament at that point. . . . After subluxation of the cataract, the extraction is completed with the aid of external pressure, by tumbling or by head-first delivery.

Knapp and numerous others have fully reviewed the advantages of intracapsular cataract extraction over the extracapsular method, with fewer and fewer dissenting voices in recent years. The "perfect cataract extraction," the goal of every ophthalmic surgeon, embraces all these advantages, which may be briefly outlined as follows:

1. A calm, cooperative patient on the operative table.
2. A more or less standardized operative technic, applicable to most types of cataract and fostering development of greater skill in both operator and assistant.
3. Routine employment of safety factors to assure a minimum of complications, both operative and postoperative.
4. A small, round, centrally placed, black pupil after operation, with minimum trauma to the iris.

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Read at the Eighty-Fourth Annual Meeting of the American Ophthalmological Society, Hot Springs, Va., May 15, 1948.

From the Department of Surgery, Division of Ophthalmology, University of California Medical School, and the United States Veterans Administration Hospital.

1. Knapp, A.: Present State of Intracapsular Cataract Operation, *Arch. Ophth.* **38**:1 (July) 1947.

5. A tight wound, well protected against leakage, prolapse of the iris and hemorrhage and allowing rapid formation of the anterior chamber and early ambulation.

6. Absence of postoperative iridocyclitis and shortened period of convalescence.

7. Minimum astigmatism.

8. Maximum visual acuity in the highest percentage of cases.

9. A grateful patient, pleasantly surprised by the absence of an anticipated ordeal and anxious to undergo operation on the second eye in order to regain the benefits of binocular vision.

It is my belief, and there is ample support for it in the literature, that these criteria are satisfied only by the performance, on a psychologically prepared patient, of cataract extraction by the intracapsular method, through a round pupil, with the employment of all modern safety measures of proved merit. It is not the purpose of this paper to present a detailed operative technic or to claim superiority of one detail over another. The use of certain methods by way of illustration should be considered an advocacy not of those methods per se but only of the fundamental principles underlying them. This study is concerned only with the basic principles involved in the mechanics or dynamics of intracapsular cataract extraction and with the methods which have proved most valuable in utilizing certain physical principles to be demonstrated.

The classic physical experiment which demonstrates that in liquids a pressure at one point transmits itself to all points within the liquid with equal force is only partially true when applied to the vitreous gel in an eyeball opened for cataract extraction. The vitreous is a tissue, and the solidier its consistency, the more readily can portions of it be "pinched off," so to speak, and made to act as isolated, smaller spheres without disturbance of the pressure ratio within the vitreous body as a whole. This fact can be demonstrated during the actual procedure of cataract extraction, on cadaver eyes, on animal eyes and by gonioscopic observation.

It is common knowledge among surgeons that the grasp of the intracapsular forceps on the anterior capsule of the lens is facilitated by pressure on the sclera sufficient to raise the vitreous pressure, thus pushing the lens forward into the jaws of the forceps. It can readily be demonstrated that the grasp on the lower portion of the lens capsule, at or under the inferior pupillary margin, preliminary to extraction of the lens by tumbling (fig. 1), is most easily obtained by applying pressure on the sclera well back toward the equator and directed upward and forward, as though "lifting" the vitreous. The lens will be seen to come forward, but it will also tilt or rotate on its horizontal axis, so that the inferior edge of the lens is anterior and against the jaws of the forceps

while the superior edge is tilted backward. A sufficiently large area of application of pressure is obtained by the Verhoeff ring<sup>2</sup> introduced deep into the lower fornix and applied flat to the globe.

On the other hand, if one wishes to apply the forceps to the upper edge of the lens, as is done in the Verhoeff<sup>3</sup> method of extraction, (fig. 2), pressure must be applied at the lower corneal limbus or even on the lower part of the cornea, and directed backward as though to push the vitreous back. This causes the lens to tilt or rotate on its horizontal axis, so that the superior edge is forward and may be straddled by the forceps while the inferior edge is depressed.

Further application of pressure in these maneuvers will cause the hydrostatic wedge of the vitreous to insert itself between the equator of

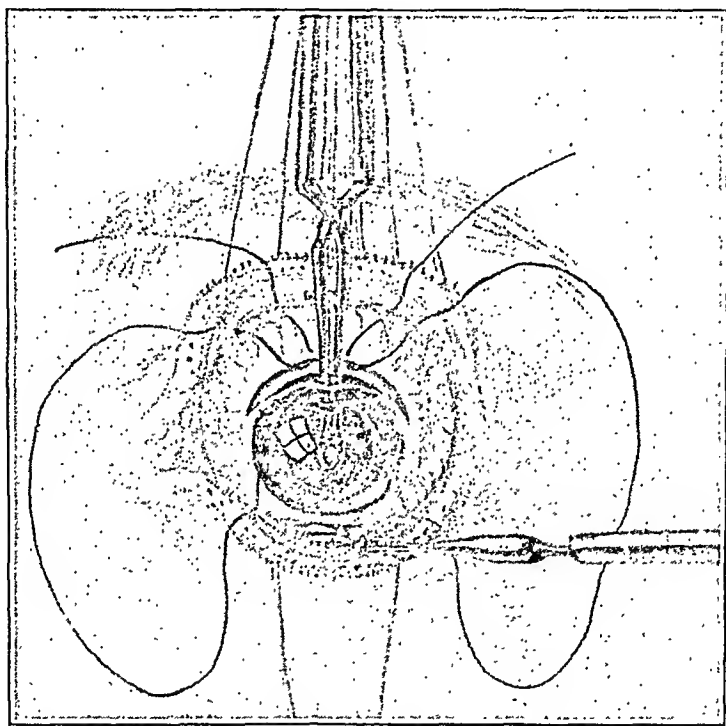


Fig. 1.—Low scleral pressure and applications of the capsule forceps in cataract extraction by tumbling.

the lens and the ciliary body and thus rupture the zonule (fig. 3 *A*), at the lower edge in the first instance and at the upper edge in the second. Light traction on the lens capsule, just sufficient to "tense" or stretch the zonule, will facilitate zonular rupture. Traction on the capsule alone without the aid of the wedge of vitreous will, of course, rupture the zonule in a certain percentage of cases, especially when it is abnormally weakened by age and the changes associated with cataract

2. Verhoeff, F. H.: *Lens Expressor*, Tr. Am. Ophth. Soc. 28:305, 1930.

3. Verhoeff, F. H.: *New Operation for Removing Cataracts with Their Capsules*, Tr. Am. Ophth. Soc. 25:54, 1927.



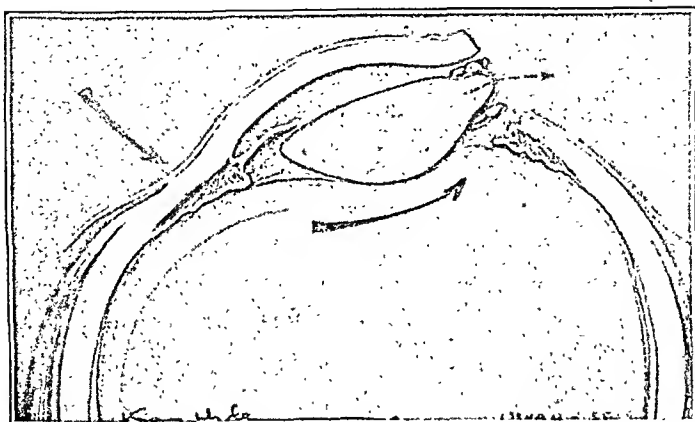


Fig. 2.—Direction of movement of the vitreous in the Verhoeff extraction with pressure on the corneal limbus.

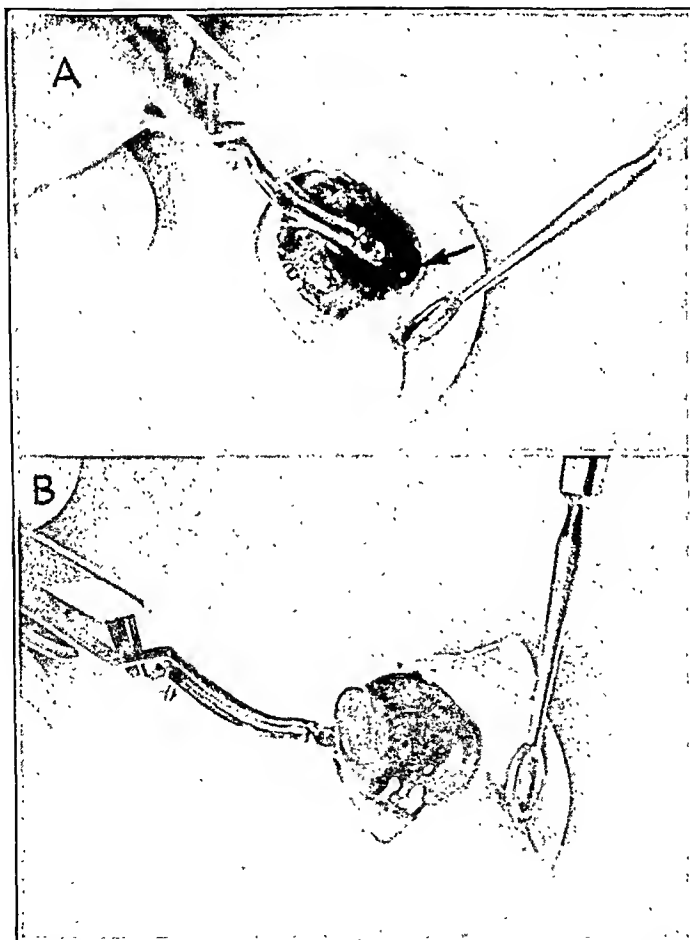


Fig. 3.—*A*, production of a wedge of vitreous between the inferior edge of the lens and the ciliary body, with rupture of the zonule. Pressure on the sclera was applied 8 mm. below the limbus. *B*, distortion of the vitreous with release of negative pressure in the hyaloid fossa as a result of low scleral pressure.

formation; but the incidence of capsular rupture is greater, the greater the ratio of traction to pressure, and one can almost state that "normally" the zonule would not be ruptured by traction alone.

After the rupture of the zonule has been accomplished, the lens must then be freed of its position in the hyaloid fossa, either by tumbling or by sliding it head first from the fossa. Barraquer<sup>4</sup> and Goldsmith<sup>5</sup> laid great emphasis on the strength of the negative pressure between the lens and the hyaloid membrane.

If the lens is tumbled, its disarticulation from the hyaloid fossa is accomplished by further application of pressure, "lifting" the vitreous below so that it presents into the lower part of the anterior chamber, pushing the lower edge of the lens ahead of it. At this point the distortion of the vitreous releases the negative pressure (fig. 3 *B*), and the lens continues to rotate on its horizontal axis. Now, for the first time, traction on the capsule sufficient to move the lens may be applied with little danger of capsular rupture, and the direction of pressure is shifted away from the vitreous and toward the cornea and the lens itself. The herniated vitreous immediately sinks back, and the final delivery of the lens is accomplished by a delicate balance between pressure and traction on the lens itself.

If the lens is to be delivered head first, as in the Verhoeff<sup>3</sup> operation, it must be freed from the hyaloid fossa primarily by traction. Application of pressure at the lower portion of the limbus sufficient to release the negative pressure in the fossa will present the vitreous ahead of the lens and into the wound (fig. 4). Pressure applied to the sclera will tend to elevate the inferior edge of the lens and depress the superior edge.

Goldsmith<sup>5</sup> objected strenuously to the head-first delivery of the lens by pressure and stated that only the fortunate previous subluxation of the lens superiorly, or early rupture of the superior zonular bundles, prevented disastrous prolapse and loss of vitreous. It should be pointed out that the Verhoeff procedure deliberately utilizes these "fortunate" factors by early zonular rupture with the forceps at the superior edge of the lens. During extraction, however, some pressure must be used, and the lens must be pressed against the posterior margin of the incision to hold the vitreous back and to avoid its loss.

The authority for the foregoing statements is the result of a gradual development of experimental work, which began several years before the war and has only recently been resumed.

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4. Barraquer, I.: *Facoerisis*, in Fisher, W. A.: *Senile Cataract*, Chicago, Chicago Eye, Ear, Nose, and Throat College, 1923, p. 34.

5. Goldsmith, J.: *Dynamics of Intracapsular Cataract Extraction*, Arch. Ophth. **29**:380 (March) 1943.

In 1930 I was afforded the opportunity of studying a patient with a very large iridodialysis opening, through which the equator of the lens and the zonular bundles were readily examined by slit lamp microscopy. Beyond the zonular barrier, which was apparently intact, the hyaloid membrane could be seen passing backward and laterally, with a vitreous of average normal consistency beneath it.

When pressure was applied to the corneal limbus, or 1 mm. on the cornea in the area of the iridodialysis, there was little or no movement in the zonular bundles or in the hyaloid membrane. When pressure was applied to the sclera at a point 6 to 8 mm. from the limbus on the same side as the area of iridodialysis, the visible vitreous seemed to move forward toward the site of iridodialysis, causing the hyaloid membrane

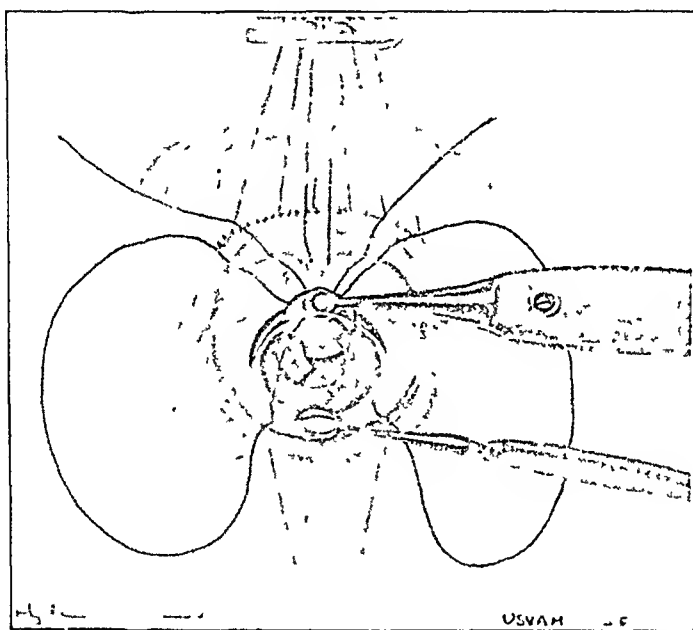


Fig. 4.—Verhoeff extraction with head-first delivery of the lens by traction and pressure on the limbus.

to bulge against the zonular membrane, which was thus placed under definite tension (fig. 5 *A*). If pressure was applied at the opposite limbus and directed backward, the hyaloid membrane and zonule in the area of iridodialysis were seen to bulge slightly, but if the same pressure was moved downward onto the sclera on the side opposite the iris opening, little or no effect was seen in the portion of the vitreous visible beneath the iridodialysis opening.

These findings were demonstrated even more clearly by gonioscopic observation and by measurement of the pressure by means of the ocular dynamometer of Bailliart. In the gonioscopic view of the angle of the anterior chamber, one could see the ciliary processes through the iridodi-

alysis opening, but only a very small portion of the origin of the zonular bundle was visible. When the 6 mm. foot plate of the ocular dynamometer was applied to the sclera in the region of the ora serrata on the same side as the area of iridodialysis and gradually increasing pressure was directed, as though to "pinch off and lift" the vitreous body, the zonular bundles suddenly appeared to bulge slightly forward into the iris opening,

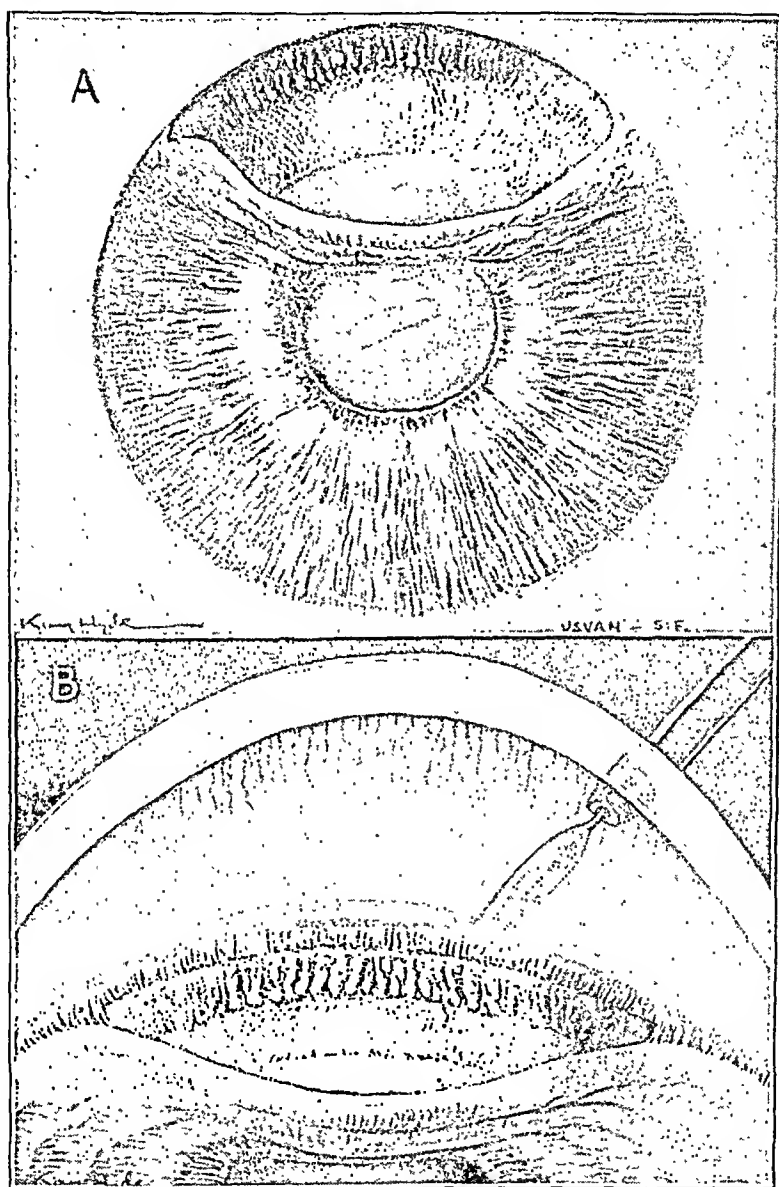


Fig. 5.—*A*, zonular tension produced by a wedge of vitreous in the iridodialysis opening, with pressure applied to the sclera on the same side 8 mm. from the limbus. *B*, gonioscopic view of production of zonular tension by a vitreous wedge in the iridodialysis opening. Pressure on the sclera was applied 8 to 10 mm. from the limbus.

and almost the entire length of the zonule became visible (fig. 5 *B*). The pressure required to demonstrate this movement was 50 Gm. Similar results have recently been demonstrated, though to a lesser extent, in a case of congenital coloboma of the iris. Even in a normal

eye, especially in a person over 50 years of age and with a low normal intraocular pressure, one can demonstrate in certain cases a slight, but definite, forward bulge of the iris in the depths of the angle under the same conditions of application of pressure (fig. 6).

Later, when an attempt was made to repair the iridodialysis defect a large keratome incision was made at the corneal limbus, thus simulating the conditions in an eye opened for cataract extraction. With the absence of an anterior chamber and with lowered intraocular pressure, it required only 20 Gm. of scleral pressure on the same side to show the forward movement of the vitreous and zonular bundles. The same amount of pressure on the opposite corneal limbus also produced tension in the visible zonular bundles, but it required 40 Gm. when applied to the opposite sclera in the region of the ora serrata to lift the entire vitreous sufficiently that movement of the zonule could be seen.

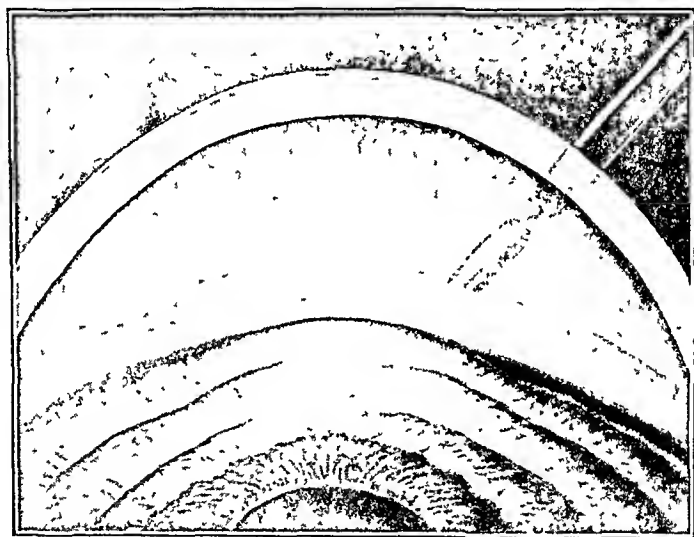


Fig. 6.—Gonioscopic view of production of a bulge of the iris by low scleral pressure. The bulge is shown as slightly exaggerated.

If an eye on which an intracapsular extraction with round pupil and peripheral iridotomy has been performed is observed with the slit lamp under these conditions of application of pressure, the movement of the vitreous in the pupillary area can be seen to follow the same general pattern, i. e., forward into the lower part of the pupil when the pressure is applied low on the sclera and across the pupillary area into its upper part when pressure is on the limbus. -

These clinical observations on living human eyes were of sufficient interest to stimulate simple experiments on enucleated animal eyes, and later on human cadaver eyes. The experiments differed from those of Goldsmith<sup>5</sup> mainly in the maintenance of an intact vitreous with zonular rupture produced by pressure. Capsular traction with the

Sinclair, Arruga or Verhoeff forceps was reduced to an amount barely necessary to guide the direction of rotation of the lens in its escape from negative pressure of the hyaloid fossa. The eresiphake was not used, as it was in Goldsmith's work. I believe that the mechanism of its action in zonular rupture is based on an entirely different basic principle, and is deserving of a separate study, already begun.

Enucleated pig eyes were studied after corneal section with and without iridectomy, after removal of the cornea with and without iridectomy, after removal of the cornea and sclera as far back as the ora serrata and after complete removal of the corneoscleral coat, with only the uveal sac, containing the retina, vitreous and lens, remaining. The reaction of these enucleated pig eyes to the applications of pressure previously outlined was exactly the same as that in living human eyes except that much greater degrees of pressure were required to produce the same effect. This difference might have been expected because of the greater solidity of the vitreous, the tougher zonular membrane and the more rigid iris tissue. It was virtually impossible to perform an intracapsular extraction through a round pupil, and rupture of the zonule by traction on the capsule was also extremely difficult. Rupture of the zonule with dislocation and complete extraction of the lens was accomplished on many eyes by the tumbling method, after complete iridectomy by pressure applied low on the sclera with herniation of the vitreous through the lower zonular bundles, but was nearly impossible with the Verhoeff maneuver, owing to the almost invariable prolapse of vitreous ahead of the lens. Because of the solid nature of the vitreous body in the pig's eye, extreme degrees of pressure were required to simulate loss of vitreous, so that conditions in these eyes could never be considered analogous to those existing in human eyes.

Extractions on rabbit eyes were entirely unsatisfactory, owing to the enormous relative size of the lens, the fragility of the zonule and the tendency to sudden total dislocation of the lens, whether accomplished by traction or by pressure or by both.

Observations on kitten eyes were quite satisfactory and agreed closely with the findings in human cadaver eyes.

The most interesting anatomic studies were those on fresh human cadaver eyes, both *in situ* and after enucleation. Six of these eyes were examined, 2 *in situ* and 4 after enucleation. One of the enucleated eyes was used with the cornea in place. After a Graefe section, a peripheral iridotomy was performed. The lips of the wound were held open about 3 mm. Gradually increasing pressure was applied to the lower part of the corneal limbus. It required only 15 to 20 Gm. of pressure to produce a definite forward tilting of the superior edge of the lens, with slight bulging of the iris and noticeable stretching of the iridotomy opening.

The area of pressure was shifted to the sclera 6 to 8 mm. below the limbus, the direction of pressure being upward and slightly forward, as though to lift the eye from the orbit. The globe was soft, so that a pressure of 30 Gm. produced a noticeable scleral dimple, but it required only 20 Gm. of pressure to produce a forward tilt of the lower edge of the lens and a bulge in the lower part of the iris (fig. 7). Further pressure, up to 40 Gm., was required to produce sudden rupture of the lower zonular bundles and forward and upward dislocation of the lens. When the scleral pressure was released, the lens settled back into place. On resumption of low scleral pressure, the vitreous presented in the lower part of the pupil, this time tilting the lens only slightly on its horizontal axis. With maintenance of this herniation of the vitreous and with the point of application slowly moved nearer the limbus, the vitreous body could be made slowly, to tumble the lens so that its inferior edge moved upward into the wound. By this time the pressure was entirely

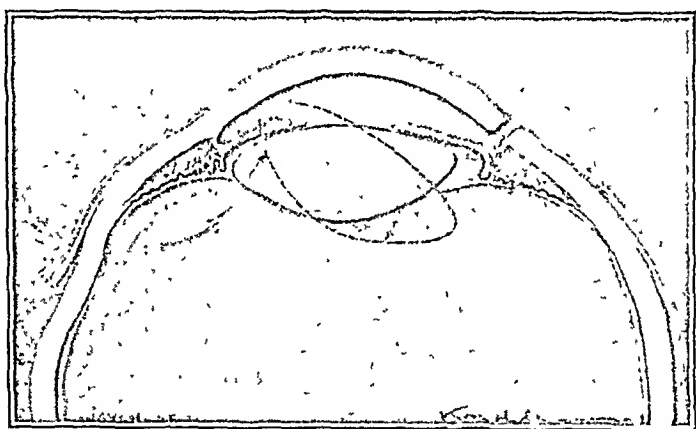


Fig. 7.—Direction of movement of the vitreous and rotation of the lens with pressure on the sclera 10 mm. from the limbus.

corneal, and final extraction of the lens was accomplished by upward massage of the cornea. This maneuver is apparently very similar to the Smith-Indian extraction. At no time during the procedure did there seem to be any great danger of prolapse of the vitreous, even though the dislocation and extraction were interrupted. If the sudden rupture of the zonule, with forward tilting of the lower edge of the lens, had been followed by a quick shift of pressure upward onto the limbus, it is felt that even less tendency to herniation of the vitreous would have been noted.

The second enucleated eye was prepared by complete removal of the cornea, and a full iridectomy was performed. With a pressure of 15 Gm. on the lower limbal area, the superior edge of the lens was tilted forward and grasped by the Verhoeff capsule forceps which straddled the equator in the area of the iridectomy. This ruptured the superior

zonular lamella. Further pressure up to 30 Gm., caused the vitreous to present in the area of the iridectomy, ahead of the lens. When the pressure was shifted downward on the sclera, the presentation of the vitreous above was lessened, but attempts to make it produce rupture of the lower zonular fibers were only partially successful, and the extraction of the lens was accomplished mainly by traction on the capsule, assisted by pressure from below while the posterior surface of the lens was held against the scleral edge of the wound to prevent the upward prolapse of the vitreous. This, as mentioned before, is the deliberate maneuver of the Verhoeff method of extraction.

The third enucleated eye was utilized to demonstrate in an exaggerated fashion the action of the wedge of vitreous in rupture of the zonule and dislocation of the lens in the tumbling method of extraction with both capsular traction and external pressure.

A Graefe section of the cornea was made, after which the lateral half of the cornea was removed and the medial half of the incision was somewhat enlarged. A band of sclera 6 mm. wide was dissected from the underlying ciliary body from 9 to 3 o'clock. A small peripheral iridotomy was performed. A very small bite of the anterior capsule of the lens was grasped at the lower pupillary border by the Sinclair<sup>6</sup> cross action forceps, and barely enough traction was exerted to place the lower part of the zonule under slight tension. When pressure was applied at the lower limbus with the foot plate of the ocular dynamometer, or with the edge or flat surface of the Verhoeff ring, the upward bulge of the vitreous was clearly shown in the area of the ciliary body above where its scleral support had been removed. When the same amount of pressure was shifted downward onto the sclera, the bulge of the vitreous in the unsupported area above was noticeably lessened, and, in fact, could easily be seen to have been brought to bear on the lower part of the zonule and the iris. In spite of the lack of support over the superior ciliary body, where a pressure transmitted through the vitreous could most easily be demonstrated, further pressure on the lower portion of the sclera readily produced an inferior wedge of the vitreous (fig. 8 *A*), which ruptured the zonule below and dislocated the lower edge of the lens forward (fig. 8 *B*). At this point slightly more traction was applied to the capsule, and with continued pressure below the lens was rotated or tumbled on its horizontal axis and freed from the negative pressure of the hyaloid fossa. Once tumbled, the lens was finally freed from its upper zonular attachment and extracted mainly by traction, but even this was assisted by moving the pressure upward into the limbal area.

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6. Sinclair, A. H. H.: Intra-Capsular Extraction of Cataract, *Tr. Ophth. Soc. U. Kingdom* 52:57, 1933.



The fourth enucleated eye was used to demonstrate Kirby's <sup>7</sup> method of head-first extraction of the lens after rupture of the inferior part of the zonule by direct point pressure on the taut zonule without utilizing the vitreal wedge.

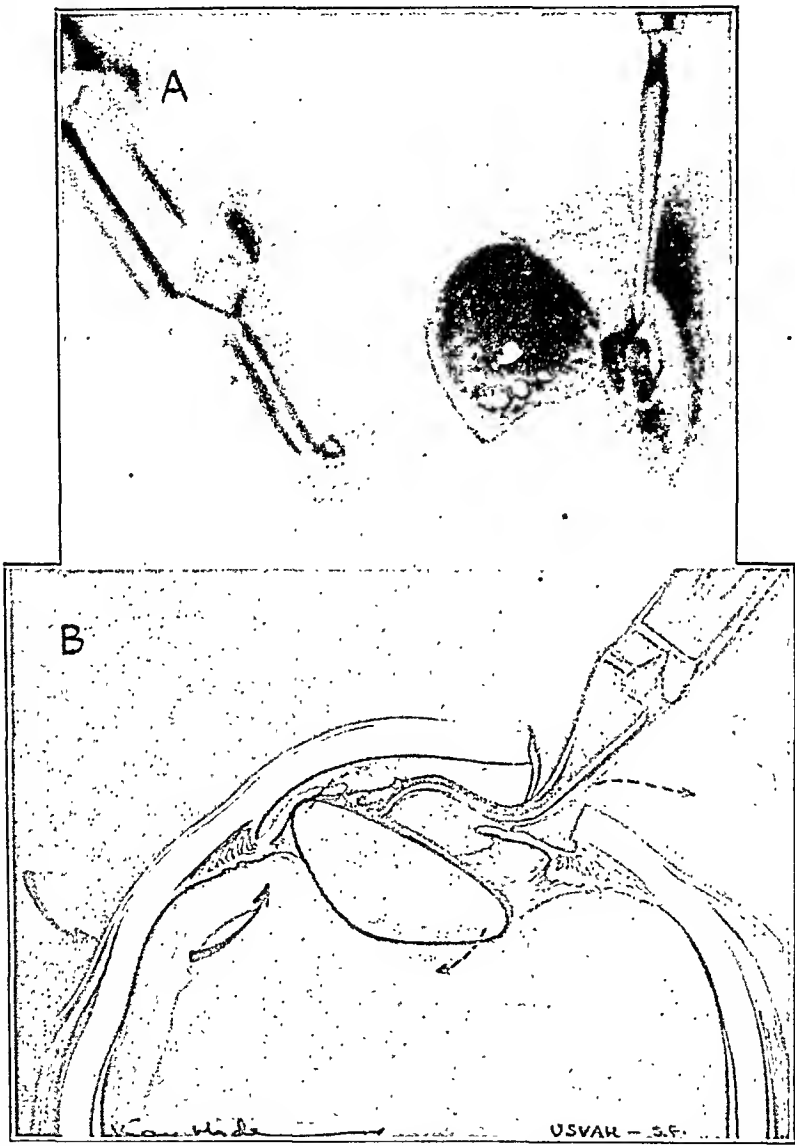


Fig. 8.—*A*, bulge of vitreous produced beneath the inferior portion of the iris by low pressure on the sclera in spite of removal of scleral support above. *B*, direction of movement of the vitreous and rotation of the lens in extraction by combined pressure and traction, with pressure exerted 8 to 10 mm. from the limbus.

7. Kirby, D. B.: The Development of a System of Intra-Capsular Cataract Extraction, *Am. J. Ophth.* **27**:124 (Feb.) 1944.

Kirby's detailed instructions as to traction at 12 o'clock combined with point pressure at 6 o'clock directly over the tensed zonule, rotation of traction to 2 o'clock combined with point pressure at 8 o'clock and rotation to 10 o'clock combined with point pressure at 4 o'clock were carefully followed. The zonule ruptured readily below, and further upward traction slid the lens head first through the wound.

Several things with reference to the action of the vitreous were noted during the procedure. Without a full iridectomy it was necessary to lift the superior edge of the lens so that on rupture of the lower part of the zonule the lens would not engage the iris above. When this was done and point pressure was applied on the lower limbus sufficient to rupture the zonule below, there was a rather pronounced bulging of the vitreous in the superior zonular area, as had been demonstrated in previous experiments. The same observation was made on 2 kitten eyes and in 1 case of extraction in the living human eye. In the latter, a full iridectomy was performed, and it is my belief that the rupture of the superior zonular area occurred through the action of the vitreous wedge, while the rupture of the inferior zonular fibers was accomplished by direct pressure. The extraction of the lens was accomplished almost wholly by traction.

The 2 human cadaver eyes which were operated on *in situ* were utilized primarily to demonstrate the mechanism of occurrence of certain operative and postoperative complications. Some of the accessory steps in intracapsular cataract extraction and their bearing on these complications will now be discussed in the light of these experiments.

#### ANESTHESIA AND LID CONTROL

The use of retrobulbar injections and akinesia has become so well established as to need little comment. It is practically universal, and the relative merits of the infiltration and the O'Brien<sup>8</sup> nerve block methods are largely a matter of the operator's personal preference. In certain prominent eyes in which there may be more than the usual danger of globe compression, it is probably wise to use both methods. It is probable that the O'Brien method gives more complete paralysis when successfully applied. On the other hand, infiltration has the advantage of producing anesthesia of the skin, which may be a valuable aid in preventing sudden movement of the patient.

For years the question of retraction of the lid has been a vexed one. Many types of speculums have been devised, but all have the disadvantage of introducing a hard metal surface between the lid and the

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8. O'Brien, C. S.: Akinesia During Cataract Extraction, Arch. Ophth. 1:447 (April) 1929.

globe and of not being quickly removable. Older operators have insisted on the importance of lid control and have preferred retractors, hand held by expert assistants.

When Horner<sup>9</sup> introduced his method of lid control by sutures (fig. 9), he was attempting to find a method which would be safe in the hands of untrained assistants. This it has proved to be, as judged by

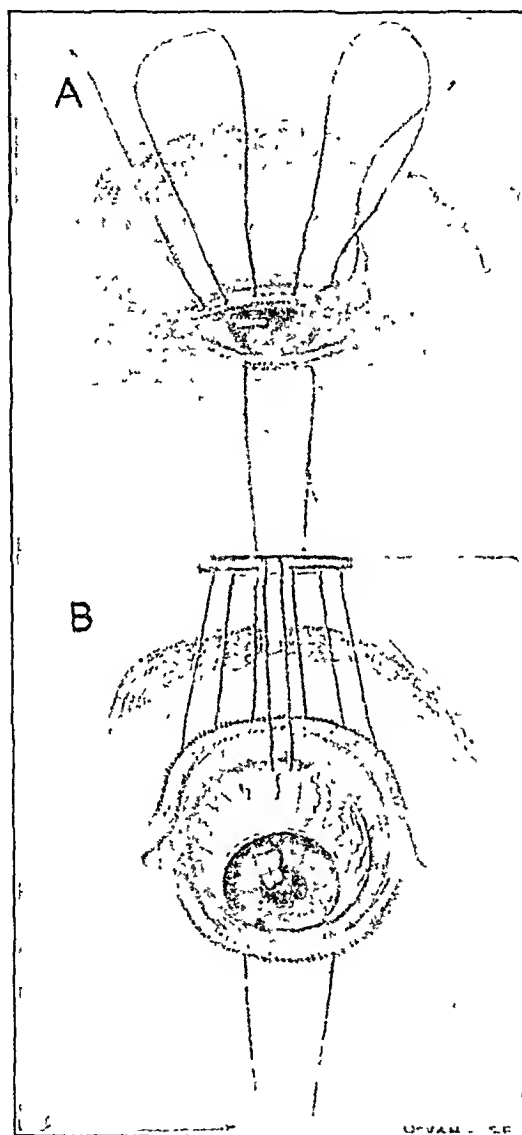


Fig. 9.—*A*, Horner lid sutures. *B*, Horner method of retraction of the lid with sutures.

experience with it at the University of California since 1931. It is felt that many potential operative complications have been avoided, and a

9. Horner, W. D.: Sutures for Lid Control in Cataract Operations, *Am. J. Ophth.* 18:33 (Jan.) 1935.

few serious complications minimized, by the quick lifting closure of the lids, which is possible only with this method of lid control.

In the cadaver eyes operated on *in situ*, it was found that even the simplest type of spring speculum required an appreciable time for its removal, that the more complicated the speculum the more difficult it was to handle and that in the presence of attempted lid closure (simulated by a purse string suture in the lid margin) the blades of the speculum produced added pressure on the globe. The lower blade of the speculum exerted its pressure at the corneal limbus, when the eye was rolled upward, in exactly the position to give maximum transmitted pressure through the vitreous into the area of the corneal wound.

The suture method of lid control had the drawback that, under too much tension, the upper lid tended to evert, causing the upper edge of the tarsal plate to indent the globe well back on the sclera in a position to produce presentation of the vitreous in the wound area. This tendency to eversion was not increased by attempted closure of the lids and could be avoided by not lifting too much on the suture. In lax-lidded persons, it might prove a source of trouble.

In the study of possible sources of postoperative wound rupture, prolapse of the iris and prolapse of the vitreous after intracapsular cataract extraction, the positions of the lids were noted on living human subjects under conditions of relaxation, moderate lid closure and tight lid closure, and attempts were made to simulate these positions in the cadaver. It was found that when the eye was closed the lid margins exerted a variable pressure on the globe at the lower corneal limbus, or merely on the lower part of the cornea. Even when the upper lid was eliminated as a source of trouble, the sharp margin of the lower lid was capable of exerting considerable linear pressure at or near the limbus in exactly the position where it would produce maximum vitreous pressure in the wound area. When this pressure was simulated either directly or by artificial tautness in the lower lid, the wound could be made to gape on either side of a corneoscleral suture, and even the slight pressure of 15 Gm. caused a movement of the iris toward the wound.

A conjunctival flap offered little resistance to this pressure. A single McLean<sup>10</sup> type of suture allowed prolapse of the iris at 10 and 2 o'clock. A modified Stallard<sup>11</sup> or mattress type of corneoscleral suture offered slightly more resistance, owing to its broader base. The most adequate protection against a measured or constant pressure up to 35 Gm. was offered by three corneoscleral sutures of McLean type or by a rather

10. McLean, J. M.: New Corneoscleral Suture, Arch. Ophth. **23**:554 (March) 1940.

11. Stallard, H. B.: Corneo-Scleral Suture in Cataract Extraction, Brit. J. Ophth. **22**:269, 1938.

wide mattress type of corneoscleral suture (fig. 10) combined with a Van Lint<sup>12</sup> type of conjunctival flap, pulled down from above.

#### IRIDECTOMY

It is fairly generally agreed that the preservation of the round pupil in intracapsular cataract extraction is much to be desired. In addition to its optical and cosmetic advantages, its greatest value, as pointed out by Knapp, lies in its action as a barrier to prolapse of the vitreous. Manipulation of the cadaver eye *in situ* showed that it required almost twice as much pressure at the lower corneal limbus to force a prolapse of the intact vitreous past an intact iris, or one on which a small peripheral iridectomy had been performed, as that required after a full iridectomy. Knapp<sup>1</sup> raised the objection that a peripheral iridectomy

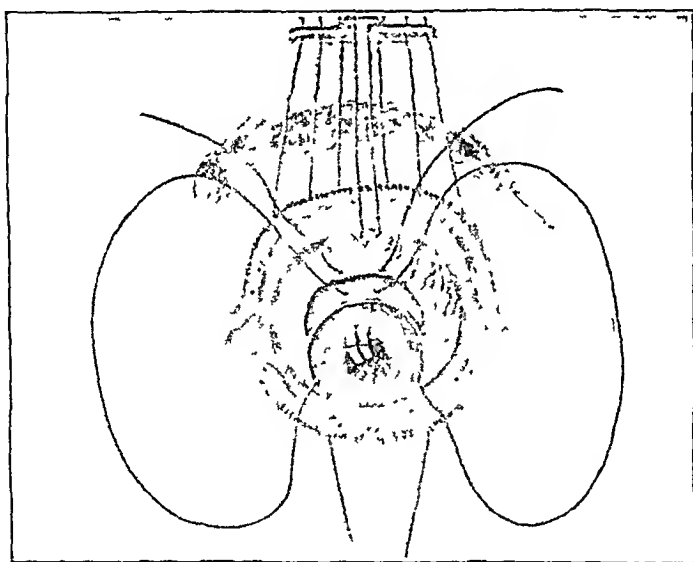


Fig. 10—Corneoscleral mattress suture and conjunctival flap.

is difficult to perform and that the possibility of cutting into the vitreous is always present. If the bite of the iris forceps is kept small and the root of the iris is tented before cutting, this can be avoided (fig. 11). The special bayonet iris forceps of Traquair<sup>13</sup> has a set screw, or wheel, between its blades, which may be preset at any desired width and will insure a small bite at the jaws.

In the cadaver eye a deliberate injury to the vitreous by a roughly performed peripheral iridectomy so changed the character of the vitreous that only one-third as much pressure was required to produce its pro-

12. Van Lint: *Astigmatisme post-opératoire dans l'extraction de cataracte avec glissement de la conjonctive*, Ann. d'ocul. **151**:418, 1914.

13. Traquair, H. M.: Personal communication to the author.

lapse after injury as before. The effect of a small nick in the hyaloid membrane is analogous to that of nicking the edge of a case-hardened glass lens. It would almost appear that the entire character of the vitreous body had been changed, so that it became semifluid and almost ceased to follow the previously outlined rules of pressure transmission. Even the slightest pressure at any point on the globe, whether near the limbus or on the sclera, produced immediate presentation and prolapse of vitreous, whereas before this injury the pressure was transmitted through the vitreous, as outlined earlier in this paper.

It is suggested that in cataract extractions in the presence of known fluid or injured vitreous pressure be applied to the globe with extreme caution and that extraction be accomplished mainly by traction.

In the presence of normal vitreous it could not be demonstrated experimentally on the cadaver eye that a double iridotomy was any more

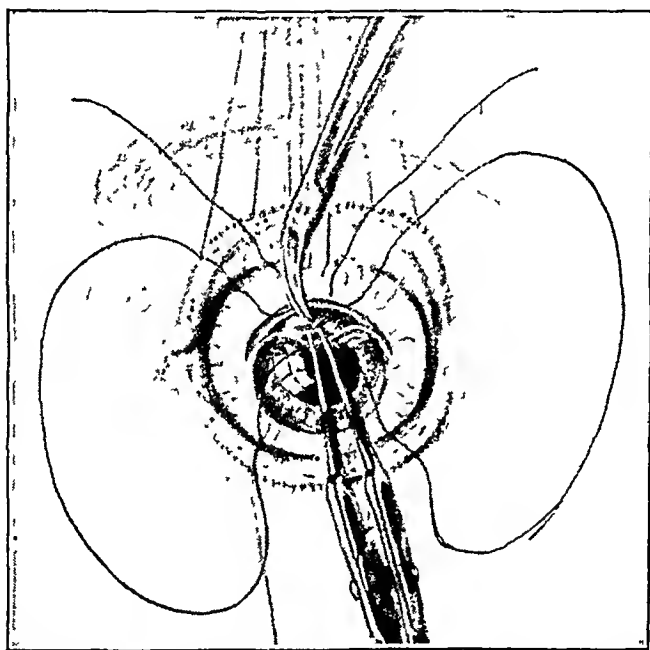


Fig. 11.—Peripheral iridotomy with small iris bite and tenting of the iris.

effective in preventing prolapse of the iris than a single one. It must be admitted, however, that these prolapses were produced by vitreous pressure rather than by sudden leakage of aqueous, such as might produce a prolapse of iris in a living eye on the fourth or the fifth postoperative day.

#### EXTRACTION BY TRACTION

Except for zonular rupture and lens extraction by phakoeresis, which involves an entirely different basic principle from that under discussion here, it is my considered opinion that zonular rupture and total extraction by capsular traction alone are very difficult and extremely uncertain. Even allowing for the known fragility of the zonule in the presence of mature cataract in the aged person, the percentage of capsular ruptures

is very high when attempts are made to extract the lens by traction alone. For this reason, most experienced operators combine traction with external pressure. On the other hand, Arruga<sup>14</sup> stated that he depended mainly on traction, and the nature of the Verhoeff<sup>3</sup> method demands preponderance of traction over pressure.

Aside from any other consideration, such as rupture of the hyaloid membrane, prolapse of the vitreous or injury to the ciliary processes, cited as disadvantages of extraction by pressure, the higher the ratio of traction to pressure, the greater the likelihood of rupture of the capsule.

#### INJECTION OF AIR INTO THE ANTERIOR CHAMBER

Ever since MacMillan<sup>15</sup> advocated the injection of air under the conjunctival flap and into the anterior chamber in trephinations for

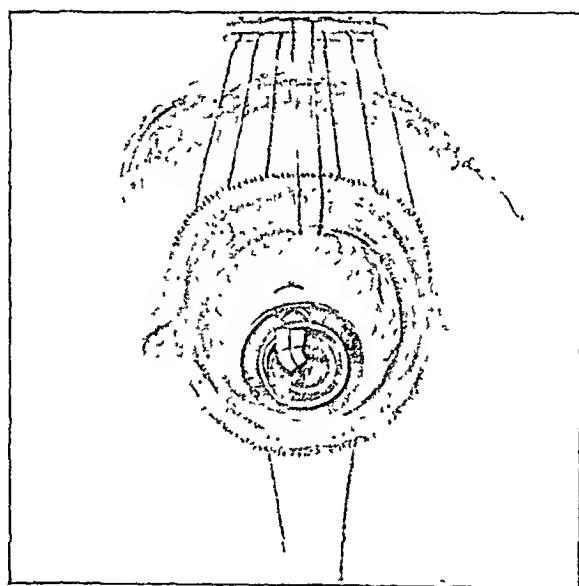


Fig. 12.—Corneoscleral suture tied and air bubble in the anterior chamber.

glaucoma, I have made this procedure routine after intracapsular cataract extraction. Besides aiding in the more rapid and even reformation of the anterior chamber, it also acts as a "cushion" to prevent prolapse of the iris in the event of postoperative pressure of the lid margins on the cornea. It was repeatedly demonstrated on cadaver eyes and on a living human eye that a pressure of 30 Gm. on the lower corneal limbus would produce a small prolapse of the iris if the anterior chamber was absent or was partially filled with fluid. If an air bubble was introduced

14. Arruga, H.: Les détails techniques de l'extraction intracapsulaire du cristallin, *Bull. et mém. Soc. franc. d'opht.* **46**:270, 1933.

15. MacMillan, J. A.: Injection of Air as Factor in Maintaining Filtration After Corneoscleral Trephining in Glaucoma, *Arch. Ophth.* **22**:968 (Dec.) 1939.

into the anterior chamber and a similar pressure was applied to the globe, the air escaped in a rush, but the iris did not prolapse into the wound. Only one precaution is necessary. If too much air is injected into the anterior chamber, producing an abnormally deep chamber, it is possible for some of the air to enter the posterior chamber and become trapped behind the iris. The application of external pressure then produces a prolapse of the iris, with the exit of air through the wound.

#### SUMMARY AND CONCLUSIONS

It is fairly generally agreed among ophthalmologists that the ideal cataract extraction from the point of view both of the patient and of the surgeon is that performed by the intracapsular method through the intact pupil, with employment of all the modern safety measures of proved merit.

In order to acquire the greatest proficiency in intracapsular cataract extraction, the surgeon should have an understanding of the physical principles underlying the dislocation and delivery of the lens.

It can be demonstrated by slit lamp microscopy, by gonioscopic observation, during actual intracapsular cataract extraction in the living eye, on animal eyes and on human cadaver eyes that the rupture of the zonular lamella of the lens is accomplished primarily by the production by external pressure of a wedge of vitreous, which is made to insert itself between the equator of the lens and the ciliary processes. This deformity of the vitreous can be produced at whatever site is desired, depending on the method and the point of application of the external pressure and on whether or not one wishes to tumble or to slide the lens from its position in the hyaloid fossa.

The normal vitreous is a tissue and cannot be considered as a fluid, in which pressure at one point is transmitted equally to all other parts.

Capsular traction facilitates dislocation of the lens by stretching the zonule, but does not normally produce its rupture.

Certain factors of safety of utmost importance in intracapsular cataract extraction may be reevaluated in the light of these basic physical principles.

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# NONSYPHILITIC INTERSTITIAL KERATITIS WITH VESTIBULOAUDITORY SYMPTOMS

Report of Four Additional Cases

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IN 1945 I described 4 patients presenting a syndrome consisting of a characteristic type of interstitial keratitis and vestibuloauditory symptoms like those of Ménière's disease and resulting, usually, in complete deafness.<sup>1</sup> Only 1 previous instance, and this one questionable, could be found from an examination of the literature. The ocular signs consisted early of a granular type of corneal infiltrate, patchy in distribution, situated predominantly in the posterior half of the cornea; late the cornea became vascularized. The keratitis was bilateral in 3 of the 4 patients and ran a characteristically chronic course, varying in its severity from day to day and from eye to eye. There was little or no reaction in the anterior chamber or the iris. The vestibuloauditory symptoms, coming on within a few days of the ocular symptoms, consisted typically of severe vertigo, tinnitus, nystagmus and rapidly progressive deafness. There was an elevated white blood cell count, and usually a mild eosinophilia, but no other evidence of systemic disease. The type of manifestations, the course of the disease, the absence of a family history and the consistently negative serologic reactions were thought sufficient evidence to rule out congenital syphilis as the cause. All the patients were young adults.

It is the purpose of the present communication to report 4 additional patients, 3 of whom were observed by me and 1 by Dr. Francis Keil. Chief interest attaches to the first patient, in whom, despite several suggestive leads, exhaustive investigation failed to disclose the cause. The fourth patient is also of interest, inasmuch as the deafness cleared up entirely.

## REPORT OF CASES

CASE 1.—*History*.—F. D., an American-born Italian, aged 24, had been under observation fourteen months. He is the second of five children, all of whom are living and well. According to the parents, both of whom are living and well, there were no miscarriages or stillbirths in the family or evidence of venereal

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From the Howe Laboratory of Ophthalmology, Harvard Medical School, and the Massachusetts Eye and Ear Infirmary.

1. Cogan, D. G.: Syndrome of Nonsyphilitic Interstitial Keratitis and Vestibuloauditory Symptoms, *Arch. Ophth.* **33**:144-149 (Feb.) 1945.

disease. Hinton tests of the parents' blood gave negative reactions. There was no history of significant ocular, aural or systemic disease in the family.

The noteworthy medical events in the patient's history were the presence of cervical lymphadenopathy in childhood and an episode of what was believed to be rheumatic fever two years prior to the present illness. This episode was characterized by sore throat, from which streptococci were cultured, followed by extensive "muscle pains," lasting about one week. He was treated at this time by sulfonamide compounds, but not by salicylates. He was subsequently found to have an enlargement of the heart and a grade 3 systolic murmur, which were attributed to this episode. Eight months prior to the onset of the present illness, while the patient was attached to the Navy in the vicinity of Japan, he lost approximately 30 pounds (13.6 Kg.) in weight over a period of three to four months, without apparent cause. He subsequently received a routine discharge from the Navy, no medical abnormality being noted. One month prior to the onset of the present illness, he had for a few days a sore throat, stiff neck and swollen glands. This condition was not treated by sulfonamide drugs.

*Present Illness.*—The present illness began, fourteen months ago, with redness of the right eye, tenderness and photophobia. Three days later, when the ocular condition appeared to be improving, severe bilateral tinnitus developed, and the patient became so dizzy that he was forced to stay in bed, acutely ill. Within one week the vertigo improved, but the patient had become profoundly deaf, first in the left ear and then in the right. During the first week, also, the left eye became inflamed, like the right eye. Beginning five days after onset, the patient was given intravenous injections of penicillin, in doses of 300,000 units daily. On the fifteenth day this medication was changed to streptomycin, one injection daily (dose not known) but penicillin therapy was reestablished on the nineteenth day, when a rash developed.

The examination to be reported took place one month after the onset of the present illness.

*Physical Examination.*—Except for signs referable to the oculoaural systems, no abnormality was noted on physical or neurologic examination.

*Ophthalmologic Examination.*—Right Eye: Vision was 20/30, with moderate ciliary redness. The cornea contained 20 to 30 ill defined, round and confluent opacities, situated in the midstroma and the posterior third of the cornea. These opacities were scattered throughout the cornea, showing no preferential involvement of the axial or limbal portion. Between the opacities the cornea was grossly clear. The opacities, which were yellowish and granular, were interpreted as infiltrate. The anterior surface of the cornea was smooth and lustrous; the posterior surface showed no folds, irregularities or deposits. Corneal sensitivity was normal. The anterior chamber was clear, showing no cells or outstanding beam. The pupil dilated well with atropine and showed no synechia. The fundus was seen fairly well and appeared normal.

Left Eye: Vision was 20/20. The findings in this eye were the same as those in the right except that at this examination they were less pronounced, the corneal infiltrates being visible only with a bright light.

Ocular motility was normal except that nystagmus was present to a somewhat greater extent than normal on conjugate gaze to either side.

*Otologic Examination.*—No nystagmus was induced by irrigating either external auditory meatus with 200 cc. of cold alcohol or by rotating the patient in a Bárány chair with the head placed in the usual position, nor did the patient have any subjective sense of being rotated. The deafness was complete.

*Neurologic Examination.*—No abnormality was found except for deafness.

*Laboratory Data.*—The urine was normal. Studies of the blood made repeatedly over a period of one month were reported as follows: The red cell count was more than 5,000,000 on several occasions. The white blood cell count (made four times) averaged 10,650 per cubic millimeter. The average differential white cell count, made seven times, was: polymorphonuclear cells, 56 per cent; lymphocytes, 26 per cent; monocytes, 6 per cent, and eosinophils, 12 per cent (with a variation of from 5 to 28 per cent). The sedimentation rates ranged from 1.3 to 1.5 mm. per minute, with corresponding hematocrit readings of 43 to 41 per cent. Serum agglutination tests were negative for brucellosis, typhoid and paratyphoid A and B. Wassermann reactions of the blood were negative. A smear from the conjunctiva showed no eosinophils, bacteria or inclusion bodies. Culture of material taken from the conjunctiva showed coagulase-positive *Staphylococcus aureus* on one occasion, but no growth on two occasions. Lumbar puncture showed normal dynamics, with a total protein content of 21 mg. per hundred cubic centimeters and a flat colloidal gold curve. The Wassermann reaction of the spinal fluid was negative. A specimen of the stool was negative for cysts. Intradermal tests with the common allergens, including molds, showed no significant sensitivity. A roentgenogram of the chest revealed nothing abnormal. Injection of serum from the patient into the abdomen of a guinea pig was without apparent effect on the guinea pig. Biopsy of tissue from the deltoid muscle showed no evidence of trichinosis, and injection into a guinea pig of material from one of the patient's cervical glands failed to produce tuberculosis. The gland itself, however, showed chronic inflammation and calcification compatible with old tuberculosis.

*Course of Illness.*—The patient was studied in the hospital for one month, during which time most of the foregoing laboratory data were obtained. The patient's temperature was at no time elevated, nor was there evidence, other than that noted in the blood studies, to suggest systemic disease.

The ocular disease continued to be characterized by patchy infiltrate in the deep corneal stroma but showed an extraordinary variation from day to day and from one eye to the other. At times one eye would show considerable infiltrate, with corresponding congestion of the globe, but these signs often cleared dramatically overnight, only to become manifest in the other eye. Yet the corneas showed no pronounced swelling and the anterior chambers no more than a faint beam, and only rarely were keratic precipitates to be found on the posterior surface of the cornea. Vascularization of the deep cornea, observed only after the disease had been present for four months, was never a conspicuous feature. Seven months after onset, the red blood cell count was 4,380,000 and the white blood cell count 12,400, with 3 per cent eosinophils. The sedimentation rate was 46 mm. in one hour. At the end of fourteen months the ocular disease was still active and continued to show its characteristic fluctuations, but at less frequent intervals.

The otologic signs, which were characterized by an incapacitating vertigo and tinnitus at the onset, consisted finally in complete deafness.

In addition to the local treatment to the eyes, the patient was given a transfusion of plasma (200 cc.) from a patient who had had the same disease one year previously. No effect on the course of the patient's ocular condition was noted. Penicillin given systemically at the onset of the disease was without benefit. After the disease had been present for eleven months, the patient was given systemically a course of riboflavin, nicotinamide and thiamine hydrochloride<sup>2</sup> with subsequent improvement in the eyes.

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2. This treatment was suggested and supervised by Dr. Miles Atkinson.

*Résumé.*—In a young man with a history of cervical lymphadenopathy and rheumatic fever, there developed within the course of a few days bilateral interstitial keratitis, tinnitus and profound vertigo. The keratitis was characterized by a granular infiltrate, arranged in a patchy distribution, situated in the deep stroma. Showing considerable variation in severity from day to day, the keratitis persisted about fourteen months and the corneas became vascularized, but at no time was the process severe enough to impair vision seriously. The initial tinnitus and vertigo disappeared within the first month as total deafness supervened and as the labyrinths became inactive. The only abnormal laboratory findings were an elevated white blood cell count (average, 10,650), eosinophilia, with a count varying from 5 to 28 per cent, and an increased sedimentation rate, 1.3 to 1.5 mm. per minute. There was no evidence of congenital or acquired syphilis. Treatment with penicillin and by transfusion of convalescent serum was without benefit, but the patient improved after multiple vitamin therapy.

*CASE 2.—History.*—R. E., a native-born Guatemalan aged 20 years, was examined fifteen months after the onset of his present illness. He is the second of 3 siblings, all of whom, as well as the father and mother, are living and well. He denied having had systemic illness other than childhood diseases, but one week prior to the onset of the present illness he had been vaccinated for smallpox.<sup>3</sup> He had not received streptomycin either during or prior to the present illness.

*Present Illness.*—The onset was characterized by tinnitus (first in the right ear, and within a few days in the left ear) and profound vertigo, accompanied with illusory movement of the environment. Deafness was first complained of three days after the onset and progressed in four months to loss of all useful hearing. The ocular symptoms, beginning five months after the onset of the aural symptoms and two weeks after an appendectomy, were characterized, according to the patient, by pain, photophobia and redness of the right eye, but no great loss of vision. The patient was examined at this time at the Mayo Clinic, with the following findings: ". . . Three pinhead-sized areas of keratitis were present on the right cornea. Two days later the keratitis was definitely worse, and the entire cornea was milky in appearance . . . the left eye remained unaffected."

From the onset to the time of the present examination, fifteen months later, the right eye continued to be intermittently inflamed and painful. The left eye had always been normal. At the Mayo Clinic the patient was treated for one and one-half months with daily injections of vitamin B preparations and for five months with intravenous injections of histamine. There was some, although slight, recovery of hearing after four months of the latter treatment.

The patient's status ten months after onset of the ocular symptoms, and fifteen months after the onset of the vestibuloauditory symptoms, is described.

*Ophthalmologic Examination.*—Right Eye: Moderate redness of the ciliary body was present. The cornea showed an arcuate opacity corresponding approximately to the border of the pupil and densest in the upper portion (11 to 2 o'clock)

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3. Since this report was submitted for publication, a description of a similar case has appeared, in which the disease also occurred one week after smallpox vaccination (Rosen, E.: Interstitial Keratitis and Vestibuloauditory Symptoms Following Vaccination, *Arch. Ophth.* **41**:24-31 [Jan.] 1949).

and in a small segment below (6 o'clock). With the biomicroscope, this opacity appeared densely granular, and was interpreted as infiltrate, with glistening particles, interpreted as cholesterol crystals. There was also a granular infiltrate of the rest of the cornea, but this was not sufficiently dense to be visible grossly. The opacities were situated predominantly in the posterior layers. The periphery of the cornea was the clearest portion. Vessels extended into the corneal stroma in its middle and posterior layers. The cornea was little, if at all, thickened, and the anterior chamber was clear. The media and fundus were normal.

*Left Eye:* The eye was entirely normal.

*Examination of Ears, Nose and Throat* (Dr. D. K. Lewis).—The nose and throat were entirely normal. There was no vestibular response with massive caloric irrigation of either ear and no response to rotation in the Bárány chair. The audiogram showed profound loss on the left with inability to comprehend speech and a hearing loss on the right averaging 60 to 65 decibels. Bone conduction was less than 50 decibels in each ear.

*Laboratory Data.*—The Wassermann and Hinton tests of the blood gave negative reactions. The blood smear showed a differential count as follows: polymorphonuclear cells, 66 per cent; lymphocytes, 27 per cent; monocytes, 3 per cent; eosinophils, 4 per cent; basophils, 0.

*Résumé.*—In a young man tinnitus and profound vertigo culminated in practically complete deafness and inactive labyrinths. Five months after onset of the aural symptoms, an inflammation developed in one eye which was recurrent for at least the next ten months. At this time there was noted in this eye a granular infiltrate in the deep cornea, having a patchy distribution and accompanied with new blood vessels and scintillating particles, thought to be cholesterol crystals. The laboratory findings were normal. There was no evidence of congenital or acquired syphilis.

*CASE 3* (patient of Dr. Francis C. Keil).—*History.*—An American woman, aged 20, was examined two weeks after the onset of the present illness. The patient is the youngest of 4 siblings, all of whom, as well as the parents, are living and well. There had been no stillbirths in the family, and Wassermann tests of the parents' blood gave negative reactions. The patient herself had always been well.

*Present Illness.*—Beginning two weeks prior to the present examination, the patient experienced an inflammation of her eyes and a vertigo which was so severe that she could not stand unaided. She rapidly became deaf.

*Physical Examination.*—No abnormality was found. There were no stigmas of congenital syphilis. The roentgenogram of the chest was normal.

*Ophthalmologic Examination.*—Vision was 20/20 in the right eye and 20/40 in the left eye.

*Both Eyes:* There were marked conjunctival and slight ciliary congestion. There were many grayish white infiltrates in the posterior half of the corneal stroma. The anterior stroma and surface of the cornea appeared normal. No cells were seen in the anterior chamber, but there was a slight aqueous flare.

*Otologic Examination.*—An audiogram showed almost complete deafness in the higher tone ranges.

*Laboratory Data.*—Wassermann and Kahn reactions of the blood and spinal fluid were negative. The spinal fluid showed normal globulin and sugar contents, a normal colloidal gold curve and a cell count of 5 per cubic millimeter. The

red blood cell count was 4,500,000 and the white blood cell count was 10,200, with a distribution as follows: polymorphonuclear type, 73 per cent; lymphocytes, 25 per cent, and monocytes, 2 per cent. The Mantoux test gave a negative reaction to tuberculin.

*Course of Illness.*—The patient received penicillin (160,000 units daily) for ten days, with little improvement. She could not be followed further, but eight months later, by telephone report, the eyes were said to have improved somewhat, although she continued to be deaf.

*Résumé.*—In a young woman there developed within a two week period bilateral interstitial keratitis and profound vertigo. The interstitial keratitis has been chronic but was not accompanied with any considerable decrease in vision. The vestibuloauditory symptoms culminated in deafness. There was no evidence of syphilis in the patient or in her family. The laboratory findings were normal except for a slightly elevated white blood cell count. The condition was little improved by systemic treatment with penicillin.

CASE 4.<sup>4</sup>—*History.*—J. G., an American professional orchestra player, aged 30, at the time of this report had been under observation seven months. He was the first-born and only surviving sibling, the others having died in infancy (ages 1 to 1½) of pneumonia (possibly tuberculous). The patient's mother died of tuberculosis when the patient was 4 years of age. One step-sister was living and well except for postmastoiditis deafness. The patient's father was living and well.

The patient had always been well. However, he had had glycosuria, presumably of renal origin, since repeated blood sugar determinations and glucose tolerance tests had shown normal values. Routine Wassermann tests of the blood several years prior to the present illness gave negative reactions.

One month prior to the onset of the present illness the patient had a stiff neck, lasting a few days. This was unaccompanied with headache or evidence of cervical lymphadenopathy so far as the patient was aware. The patient had had no medication for this or any other condition prior to the onset of the present illness.

*Present Illness.*—The onset was characterized by redness and watering of the left eye. This was followed in a few days by severe vertigo, with illusory movement of the environment, vomiting, buzzing in the ears and progressive deafness. The last two symptoms applied to both ears but were most pronounced on the right side. Within a few days after onset the right eye became involved, and corneal opacities developed, with considerable photophobia and blepharospasm. The patient's local physician made the diagnosis of Ménière's disease. He was further studied at the Lawrence General Hospital, where a diagnosis of interstitial keratitis and labyrinthitis was made. Except in the eyes and ears, physical examination revealed nothing unusual. A lumbar puncture was done at this time, and examination of the cerebrospinal fluid showed a negative Hinton reaction, 74 mg. of sugar and 32 mg. of total protein, per hundred cubic centimeters, and 2.5 white cells per cubic millimeter. Roentgenograms of the chest and skull showed nothing abnormal.

During the first two months of the disease the watering, redness of the eyes and blurring of vision continued with moderate severity, the condition showing

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4. Dr. Karl Riemer gave me the privilege of seeing and following this patient.

characteristic variations from day to day and possibly being worse in hot weather. The patient remained partially deaf, with what was described as a "marked hearing loss in the right ear and moderate loss in the left ear, of the perceptive type of deafness," but the loss of equilibrium, which had been profound at first, had improved somewhat in the interim. Examination of the eyes two months after the onset showed considerable ciliary injection of both eyes, with yellowish infiltrates, arranged in ill defined patches, in the deep stroma. Nevertheless, there were no precipitates on the posterior surface of either cornea, little swelling of the cornea and no perceptible synechias. The cornea showed beginning vascularization in a lamina immediately in front of Descemet's membrane. Treatment during the first two months had consisted of administration of sulfonamide drugs systemically at the start and continued mydriasis. The Wassermann reactions of the blood at this time were again negative.

Approximately three months after the onset, the patient's hearing suddenly returned. He awoke one morning and found he could hear normally, and this was corroborated by an audiogram. Since this time the only vestibuloauditory symptoms have been an occasional spell of vertigo with illusory movement of the environment, lasting only a few seconds. The eyes remained irritable, however, and examination showed the same objective signs as before except that the vascularization had extended farther toward the axis of the cornea. There was still no perceptible reaction in the anterior chamber. Although the Wassermann reactions of the blood and spinal fluid were negative, the patient was given a series of injections of a bismuth preparation.

Approximately four and one-half months after the onset, the eyes began to feel less irritable, and on examination five months after the onset the corneal infiltrate was less marked, the eyes were whitening out and there was obviously much less photophobia than formerly. The ocular status at this time was characterized by deep corneal opacities, which were barely perceptible grossly, and deep, apparently quiescent, vascularization of the corneas.

*Résumé.*—In a young man there developed within a few days photophobia, blepharospasm, deafness and vertigo with illusory movement of the environment and vomiting. Examination of the eyes showed a deep infiltration of both corneas with a characteristic patchy distribution, culminating in vascularization of the corneas but unaccompanied with any appreciable reaction in the anterior chambers. The deafness, which was never complete, spontaneously resolved approximately three months and the eyes began to show improvement four and a half to five months, after the onset.

#### COMMENT

There can be little reasonable doubt that the clinical picture in the 4 cases presented here accorded with the syndrome previously described as nonsyphilitic interstitial keratitis with vestibuloauditory symptoms. They illustrate the characteristic day to day fluctuation in the severity of the ocular process, which was insufficiently emphasized in the previous report but which is a major feature distinguishing this type of interstitial keratitis from that due to congenital syphilis. Other distinguishing features of the ocular reaction in this syndrome are the patchy distribution, the relative mildness of the process, the absence of any striking intra-

ocular involvement, the maintenance of a relatively normal posterior surface of the cornea, the absence of any marked swelling of the cornea and the chronicity. The vestibuloauditory reactions are characterized by symptoms like those of Ménière's disease with rapid development of deafness; this is unlike the vestibuloauditory symptoms in congenital syphilis, in which there is a slow evolution of deafness without appreciable vertigo.

No conclusive evidence indicating the etiologic factors in this syndrome was apparent. One patient had a recent history of rheumatic fever and cervical lymphadenopathy, and 1 patient had had vaccination for smallpox one week prior to the onset of the present illness. The type of corneal infiltrate, the elevated sedimentation rate and the relative leukocytosis of the blood suggest a bacterial, rather than a virus, disease, but cultures have not been informative. The eosinophilia, which was marked in 1 of the present patients, appears to be characteristic of the entity, but there is no indication of what its significance is. The vertigo, and deafness suggest a streptomycin-induced reaction, but only 1 of the patients gave a history of having received streptomycin, and this only after the onset of the disease.

Treatment of the disease in 1 patient with a single transfusion of convalescent plasma was without benefit. Prolonged treatment with intravenous injections of histamine may have had a slightly beneficial effect on the hearing of 1 patient. Treatment of 1 patient with a multiple vitamin preparation appeared to benefit the ocular reaction late in the course of the disease. Multiple vitamin therapy had not benefited other patients early in the course of the disease, and there was no evidence of systemic vitamin insufficiency in any of the patients.

#### SUMMARY

A description is given of 4 additional cases of what is believed to be the syndrome previously described as nonsyphilitic interstitial keratitis with vestibuloauditory symptoms. The interstitial keratitis was bilateral in 3 of the new cases and unilateral in 1 case. It was characterized by patchy, granular infiltrates in the deep stroma, which varied from day to day, unaccompanied with any conspicuous intraocular reaction. The vestibuloauditory symptoms were similar to those occurring in Ménière's disease and were followed by practically complete deafness in 3 of the patients, with complete recovery of the deafness in 1. The onsets of the ocular and of vestibuloauditory symptoms were within a few days of each other in 3 of the patients but were separated by a five month interval in 1 patient. As in the previously reported series, all 4 patients were young adults. All had a leukocytosis, 1 of whom had a significant eosinophilia. No conclusive evidence was ascertained regarding etiology or specific treatment.



## DIRECT SURGERY OF PARETIC OBLIQUE MUSCLES

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IT IS THE purpose of this paper to discuss seven years' experience with direct surgery of the underacting superior oblique muscle and eight years' experience with direct surgery of the weak inferior oblique muscle. Although the long-standing fear of oblique muscle surgery was gradually yielding to successful demonstrations of weakening operations on the inferior oblique muscle, it remained for Wheeler,<sup>1</sup> in 1935, to show that surgical correction of the superior oblique could be performed and that the underacting inferior oblique could be strengthened. Before his paper, and even after it, attempts to compensate for pareses of the oblique muscles were usually made on the vertical rectus muscles, if at all.<sup>2</sup> The influence of von Graefe's<sup>3</sup> frequently quoted interdiction of direct surgery of the oblique muscles was still strong.

The anatomy and physiology of the oblique muscles have been so adequately reviewed and discussed, especially in the recent papers of Fink<sup>4</sup> and Adler,<sup>5</sup> that reiteration here would be superfluous. Only choice of operation, operative technics and operative results will be discussed in this paper.

### PARESIS OF THE SUPERIOR OBLIQUE MUSCLE

There are obvious objections to surgical procedures on the vertical rectus muscles of the same eye to correct the effects of weakness of the superior oblique. Weakening operations on the superior rectus may

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1. Wheeler, J. M.: *Am. J. Ophth.* **18**:1, 1935.

2. Landolt, E.: *Am. J. Ophth.* **6**:93, 1923. Snell, A. C.: *Injuries of Superior Oblique Muscle*, *Arch. Ophth.* **48**:111 (March) 1919. Banister, J. M.: *Am. J. Ophth.* **2**:537, 1928. Savin, L. H.: *Proc. Roy. Soc. Med.* **27**:1058, 1934. Jaensch, P. A.: *Klin. Monatsbl. f. Augenh.* **97**:807, 1936. Bielschowsky, A.: *ibid.* **69**:611, 1922. Dunnington, J. H.: *Am. J. Ophth.* **14**:1140, 1931.

3. von Graefe, A., in Graefe, A., and Saemisch, T.: *Handbuch der Augenheilkunde*, Leipzig, Wilhelm Engelmann, 1898, vol. 8, p. 84.

4. Fink, W. H.: *Tr. Am. Acad. Ophth.* **50**:269, 1946.

5. Adler, F. H.: *Tr. Am. Ophth. Soc.* **43**:255, 1945.

tend to neutralize the vertical discrepancy in the primary position but have two distinct disadvantages. They add to the already existing imbalance in lower nasal gaze a new and unnecessary defect in upper temporal gaze. They tend also to increase the torsional defect by weakening the other intorting muscle. Strengthening operations on the inferior rectus have similar disadvantages, calling on a lower temporal hypotropia to meet the defect of a lower nasal hypertropia and increasing the torsional defect.

Weakening of the inferior oblique of the same eye is less unsatisfactory, for it tends to balance the torsional defect; but, instead of correcting the lower nasal hypertropia, it attempts to neutralize it by superimposing an upper nasal hypotropia.

All the aforementioned procedures are in conflict with the very important and useful cardinal principle enunciated by Duane<sup>6</sup> and reemphasized by White,<sup>7</sup> that muscle surgery should be confined to the field of action of the defective muscle. In this connection, the only two satisfactory procedures are direct strengthening of the paretic superior oblique and weakening of inferior rectus of the opposite eye. Of these two approaches, the first is to be preferred, for three reasons. It attempts to restore normal relations of motor function instead of balancing an existing defect by adding a second defect. It avoids the difficulties with altered lid fissures inherent in any extensive surgical work on the vertical rectus muscles and also avoids the difficulties involved in interference with the ligament of Lockwood.<sup>8</sup> It tends to restore better muscle balance in the position of depressed convergence, so important in reading and other pursuits of modern life.

#### TECHNIC

With this reasoning in mind, my colleagues and I have been making attempts at direct strengthening of paretic superior oblique muscles since 1941. The first technic adopted was a modification of Wheeler's.<sup>1</sup> His technic, while described as "advancement," is not advancement in the usual sense of the term but, rather, a folding and advancement of the middle of the tendon—a compromise between advancement and tucking. Because of the fear that his technic might result in failure of permanent adhesion of the smooth tendon surface to the sclera, a true tuck was performed at the scleral insertion of the muscle in inverted fashion, with the tucked loop buried beneath the tendon (fig. 1A). This fear seems to have been justified by the subsequent experiences of McGuire.<sup>9</sup> This modified technic was successful, as will be illustrated in the case reports to follow, but appeared to have room for improvement. The amount of reaction following the extensive exposure and dissection was more than desirable. Removal and replacement of the superior rectus seemed undesirable.

6. Duane, A., cited by White.<sup>7</sup>

7. White, J. W.: *Tr. Pacific Coast Oto-Ophth. Soc.* **26**:112, 1941.

8. Fink, W. H.: *Ligament of Lockwood in Relation to Surgery of the Inferior Oblique and Inferior Rectus Muscles*, *Arch. Ophth.* **39**:371 (March) 1948.

9. McGuire, W. P.: *Tr. Am. Ophth. Soc.* **44**:527, 1946.

A second method was then devised to avoid interference with the superior rectus and to reduce the amount of dissection. A conjunctival incision was started at the nasal end of the tendon of the superior rectus and carried nasally and posteriorly. With the globe turned down by a muscle hook or a traction suture placed beneath the superior rectus tendon, a hook was introduced between Tenon's capsule and the sclera and passed backward in the orbit about 1 cm., until it could be turned to engage and withdraw the tendon of the superior oblique. (This approach to the tendon has since been described by Berke<sup>10</sup> in his operations of tenotomy and tenectomy.) The mobilized tendon was then tucked in the usual fashion (fig. 1*B*) and allowed to retract. This method was satisfactory in my hands, but a colleague<sup>11</sup> reported his unfortunate experience when he placed a tuck too close to the trochlea and produced abrupt limitation of nasal depression of the eye.

With this potential difficulty in mind, a third technic, having the advantages of the first two, was devised. This method proved most satisfactory and is still in use today. Conjunctiva and Tenon's capsule are incised at the temporal border of the superior rectus tendon, and the incision is carried temporally and posteriorly. With the superior rectus tendon on a muscle hook or traction suture, the eye is turned strongly downward and nasally.

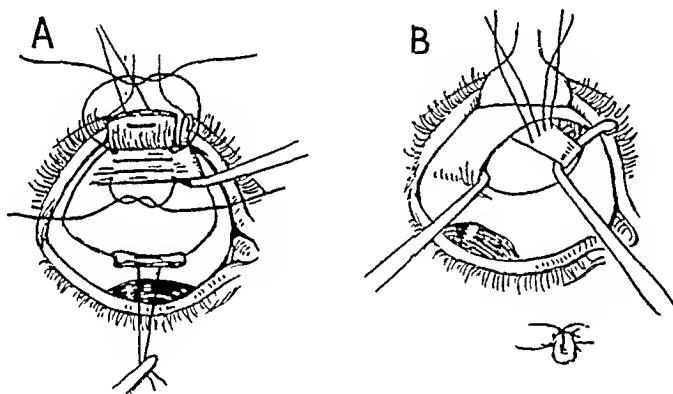


Fig. 1.—*A*, inverted tucking of superior oblique with temporary removal of superior rectus. *B*, tucking of superior oblique by nasal approach without disturbing the superior rectus.

In some eyes the insertion of the superior oblique muscle is thus exposed to direct sight. In others the belly of the superior rectus may be lightly retracted to allow direct exposure. The superior oblique tendon is then withdrawn from beneath the superior rectus, freed from the light attachments to its sheath and tucked to the desirable amount (fig. 2*A*). If desired, the apex of the tucked loop may be anchored to the sclera (fig. 2*B*). This anchoring is not designed to be the main support, as in Wheeler's<sup>1</sup> technic, but is intended merely to keep the loop in proper position. Chromic surgical gut, buried silk and buried nylon sutures have all been used satisfactorily. The amount of postoperative reaction is still somewhat greater than that encountered in the usual operations on the rectus muscles, but definitely less with Wheeler's method or with the first technic described. Tucking has been chosen rather than resection, because the tendon of a very parietic superior oblique muscle is often so thin and stringy that resection sutures

10. Berke, R. N.: *Tr. Am. Ophth. Soc.* 44:304, 1946.

11. Personal communication to the author.

may conceivably pull out. True advancement has not been used, for the same reason, because the amount of further posterior dissection and exposure seems unnecessary and because of a reluctance to do too heavy suturing in the region of the macula.

### RESULTS

In all, 19 tucking operations have been performed on 19 superior oblique muscles in 15 patients since 1941. The results have been generally satisfactory. Six were done by the technic illustrated in Figure 1 *A*, 4 by that in figure 1 *B* and 9 by that in figure 2. There were no serious complications, and the amounts of correction obtained by direct operation on the paretic superior oblique were gratifying. In some instances, it was necessary to perform supplementary recession of a secondarily contracted inferior oblique when the paresis was of long standing or a small recession of the opposite inferior rectus to

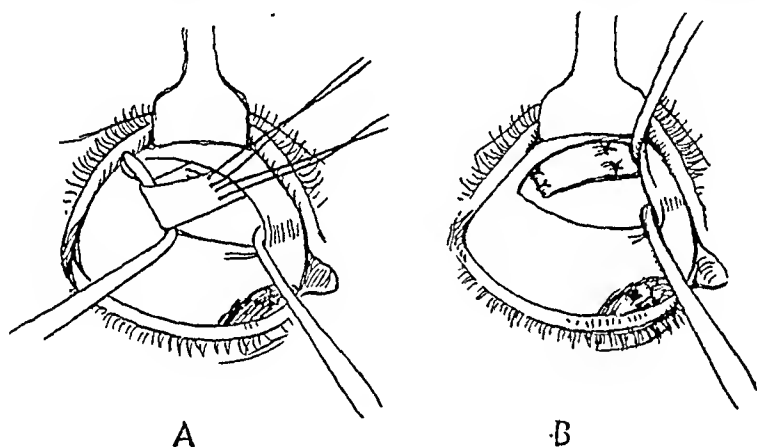


Fig. 2.—*A*, tucking of the superior oblique by temporal approach, without disturbing the superior rectus; *B*, tip of tuck anchored to sclera.

achieve final satisfactory results. No clearcut relation was found between the length of the tuck and the amount of correction obtained. It seems best to estimate the amount required by the appearance and feel of the muscle on the hook and then to adjust it to the proper tension. An estimate of this proper tension is gained by careful exposure and by testing of normal superior oblique muscles during routine enucleations.

Five cases are cited as examples of situations in which tucking of the superior oblique is useful. The other cases were similar.

### ILLUSTRATIVE CASES

*CASE 1.—Congenital Paresis of Superior Oblique Muscles with Head Tilt, Vertical Diplopia and Asthenopic Symptoms.*

P. L., a 15 year old schoolgirl, had had head tilt to the right, headaches brought on by reading, occasional vertical diplopia and occasional deviation up and out of the left eye when very tired, as long as she could remember. Her mother stated

that for the first five years of the patient's life the left eye had turned up and in, until an anterior tenotomy of the left inferior oblique muscle had been performed. This first operation had resulted in some cosmetic improvement. On Nov. 25, 1944 she had 20/20—vision in each eye. The only abnormalities were in function of the extraocular muscles. The results of general physical examination and laboratory studies were normal. She customarily held her head tilted toward the right shoulder. There was definite lag in excursion of the left superior oblique (fig. 3) Muscle balance measurements, expressed in prism diopters, by cover test were <sup>12</sup>

X 6  $\Delta$   
LH 18  $\Delta$

X 6 LH 12  $\Delta$   
X 12 LH 16  $\Delta$

X 10  $\Delta$   
LH 4  $\Delta$

X 4  $\Delta$   
LH 45  $\Delta$

X 6  $\Delta$   
LH Trace

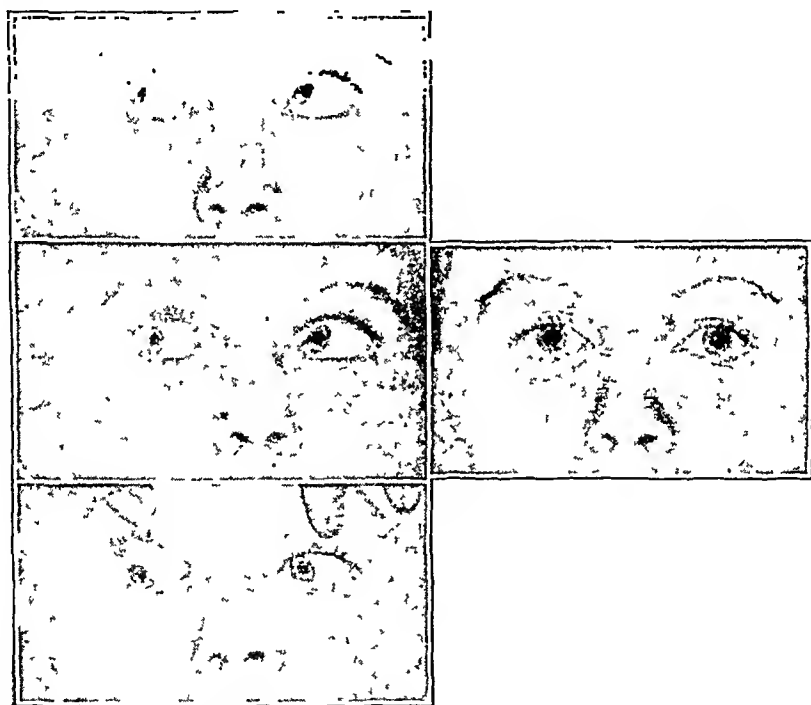


Fig. 3 (case 1).—Congenital paresis of left superior oblique (preoperative appearance).

With a red glass, diplopia could be elicited, increasing on the patient's looking to the right and down, with the left image lower. Fusion was good. A diagnosis of congenital paresis of the left superior oblique muscle was made.

On Sept. 6, 1945, with the patient under thiopental sodium (pentothal sodium®) anesthesia, a 12 mm. tuck in the left superior oblique muscle was performed by the third method described. The postoperative reaction was only moder-

12. In this tabulation, and in the accompanying tabulations, X and X' indicate exophoria for distant and near vision; XT and XT', exotropia for distant and near vision; S and ST and S' and ST', esophoria and esotropia for distant and near vision, respectively; RH and RH', right hyperphoria for distant and near vision, and LH and LH', left hyperphoria for distant and near vision.

ate, but an overcorrection persisted for nearly a month. At the end of this time satisfactory muscle balance was obtained and has been maintained ever since (fig. 4). All her symptoms have disappeared, and she has been able to enter college and study for long periods without discomfort, diplopia or head tilt. The last muscle balance measurements, made on Sept. 23, 1947, were:

X 2 $\Delta$	X 1 $\Delta$ LH 2 $\Delta$	X 4 $\Delta$
	X 7 $\Delta$	
X 2 $\Delta$		X 3 $\Delta$
LH 4 $\Delta$		

*CASE 2.—Recurrent Amblyopia After Operation on Horizontal Rectus Muscles Overcome by Operation on Congenitally Paretic Superior Oblique.*

M. B., a 5 year old boy, had first been seen by an ophthalmologist in Baltimore for convergent strabismus and amblyopia ex anopsia of the right eye. After

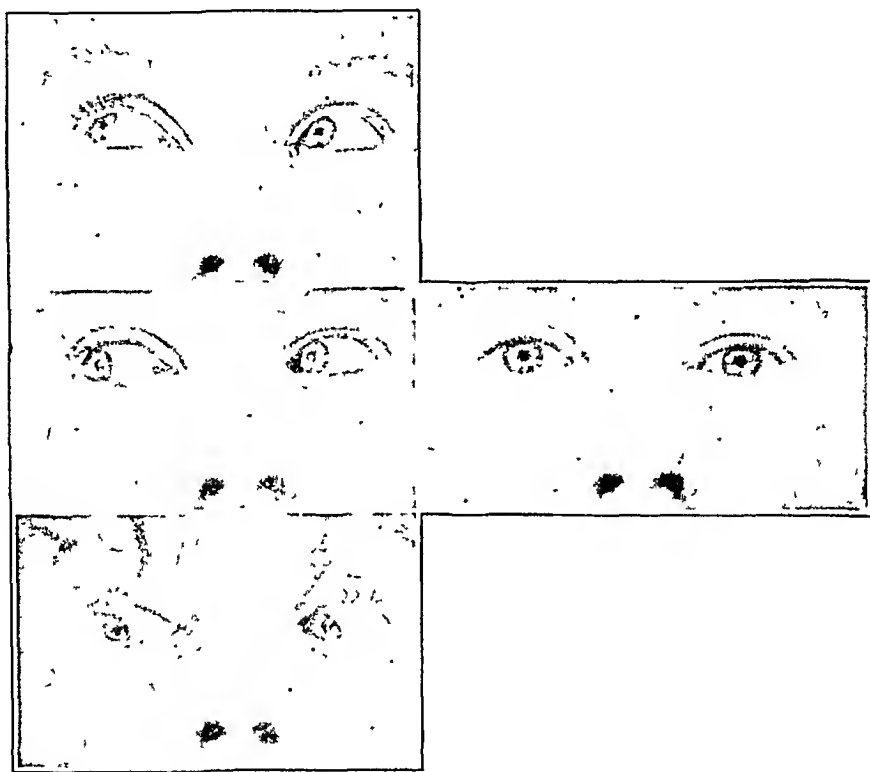


Fig. 4 (case 1).—Improvement in function of superior oblique after tucking.

correction of the amblyopia by training and occlusion, recession of the right medial rectus and resection of the right lateral rectus in 1940 had produced a good cosmetic result. Shortly thereafter his family moved to New York.

Examination on April 28, 1941 showed the corrected visual acuity to be 20/70 in the right eye, 20/20 in the left eye. There were operative scars over the horizontal rectus muscles of the right eye, but the eyes were otherwise structurally normal. Ocular excursions showed a lag in the right superior oblique (fig. 5). There was no pronounced head tilt and diplopia was not elicited. Muscle balance measurements by cover test were:

XT 10 $\Delta$	XT 5 $\Delta$ RH 4 $\Delta$	XT 7 $\Delta$
	ST'—XT'	
XT 7 $\Delta$		RH 12 $\Delta$
RH 4 $\Delta$		



esophoria and right hyperphoria becoming a right hypertropia and right esotropia on removal of the glasses, and often with them on. On excursions there was obvious weakness of the right superior oblique muscle. When the eyes were straightened with glasses, the head tilted to the left. When fusion was broken, the head straightened. Muscle balance measurements were:

ST 14△		ST 16△
RH 5 △		RH 12△
	ST 12△ RH 9 △	
	ST' 18△ RH' 12△	
ST 20△		ST 20△
		RH 26△

On Aug. 12, 1943, with the patient under ether anesthesia, a 10 mm. tuck of the right superior oblique was performed by the second method described. The post-operative reaction was moderate, and the immediate overcorrection soon subsided. From that time until Oct. 13, 1944, when the patient was last seen, function of the superior oblique was good, and the eyes were held straight without glasses at all times. Muscle balance measurements were:

S 6 △		S 8 △
	S 4 △	
	S' 12△ RH' 1△	
S 10△		S 10△
		RH 4 △



Fig. 6 (case 2).—Function of paretic superior oblique muscle in both eyes restored by tucking.

*CASE 4.—Bilateral Paresis of Superior Oblique with Convergent Strabismus (Divergence Insufficiency).*

S. S., a 33 year old woman, came to the clinic complaining of "crossed eyes." In 1937 she had had a recession of her left medial rectus for the same complaint. Vision was 20/30 + in the right eye and 20/200 in the left eye. Except for a small scar over the left medial rectus, the eyes were structurally normal. There was obvious convergent strabismus with underaction of both superior oblique muscles. No head tilt or diplopia was noted. Amblyopia in the left eye could not be improved. Muscle balance measurements were:

ST 37△		ST 30△
RH-LH△		RH 6 △
	ST 56△ RH-LH	
	ST' 40△ RH'-LH	
ST 40△		ST 50△
LH 12△		RH' 16△

A diagnosis of divergence insufficiency with bilateral paresis of the superior oblique was made. On Nov. 11, 1943, with the patient under general anesthesia,



the right lateral rectus was resected 10 mm. and the right superior oblique tucked 12 mm. by the first method. The left lateral rectus was resected 9 mm. and the left superior oblique tucked 10 mm. by the third method. There was definitely more reaction after operation in the right eye. After the reaction subsided, the eyes settled down to good position and excursions in all fields, with good depression by the superior oblique muscles (fig. 6). Muscle balance measurements on July 3, 1945 were:

XT Trace	XT 1Δ RH 1Δ	XT Trace
LH Trace	ST' 2Δ RH' 3Δ	RH 4Δ

*CASE 5.—Convergent Strabismus with Pareses of Superior Rectus and Superior Oblique in the Same Eye.*

M. K., a 5 year old girl, had had bilateral recession of the medial rectus for convergent strabismus at the age of 3. The eyes had appeared straight for about a year but then converged again. The refractive error was minimal. Vision



Fig. 7 (case 5).—Congenital pareses of right superior rectus and right superior oblique (preoperative appearance).

was 20/30 in each eye. Fixation was made with the right eye in all fields to the right, and with the left eye in all fields to the left. There were incomplete excursions in the field of the right superior rectus and the right superior oblique (fig. 7). Measurements by screening were:

ST 25Δ	ST 25Δ
LH 10 Δ	RH 8 Δ
	ST 25Δ RH 5Δ
	ST' 28Δ RH' 7Δ
ST 24Δ	ST 28Δ
LH 8 Δ	RH 12Δ

In the field of the paretic right superior rectus, fixation was performed by the paretic eye with secondary deviation of the left inferior oblique. In the field of the paretic right superior oblique fixation was performed by the sound eye. Surgical intervention was planned accordingly; on May 8, 1944 both lateral rectus muscles were resected 9 mm., the left inferior oblique was receded 8 mm. and the right superior oblique was tucked 8 mm., by the third method. The post-

operative reaction was slight and the result satisfactory. Most recent measurements, on Oct. 13, 1945, were:

RH Trace

R11 4-L11 3Δ

S 5Δ

RH' 2-LH' 3Δ

O

O

### PARESIS OF THE INFERIOR OBLIQUE

In like manner, the proper approach to a paretic inferior oblique muscle can be deduced. In this case, however, the problem of a muscle with important function in the reading position does not enter into the discussion. The principle of operating on the paretic muscle when the sound eye fixes in the field of the defect and weakening the secondarily deviating muscle when the paretic eye fixes in that field should be more strongly adhered to. Exception may have to be taken when the secondary deviation of a superior rectus is extreme and would require excessive recession of that muscle with resultant retraction of the upper lid. Such a situation is better faced by splitting the correction between strengthening the paretic inferior oblique and weakening the superior rectus of the opposite eye, even though all fixation is accomplished with the paretic eye. If too large a recession is performed on a superior rectus muscle, recession of the levator may later be required for cosmetic purposes. It also seems better, when such a divided surgical procedure is chosen, to perform the operation in two stages, with strengthening of the paretic inferior oblique as the first stage and with recession of the secondarily overacting superior rectus reserved to take up the balance. Isolated pareses are less common in the inferior oblique than in the superior oblique muscle, and these pareses are more apt to be found in complex combinations.

### TECHNIC

The first approach tried was Wheeler's<sup>1</sup> advancement of the origin of the inferior oblique over the anterior rim of the orbit. Because results were erratic, a search was made for a more satisfactory technic. Because of the success with tucking of the superior oblique, tucking of the inferior oblique at its scleral insertion was next attempted.

This method was abandoned after 8 tucking operations because the bulk of the tuck tended to collide with, and adhere to, the overlying lateral rectus muscle. The next approach was resection at the insertion, after White.<sup>13</sup> This procedure seemed to obviate some of the disadvantages of the tucking but, in common with it, had an outstanding fault. Small corrections could be readily achieved, but large resections gave little or no further correction. The explanation of this strange phenomenon seems to be in the anatomy of the muscle itself. With a very short, practically negligible, tendon at its insertion the inferior oblique cannot be resected extensively without destroying enough of the contractile tissue of the muscle belly to defeat the purpose of the large resection. After 22 resections, it

13. White, J. W.: Paralysis of Superior Rectus and Inferior Oblique Muscle of Same Eye, *Arch. Ophth.* **27**:366 (Feb.) 1942.

was determined that this operation must be reserved for cases requiring only small corrections.

The obvious procedure, then, seemed to be advancement of the insertion of the muscle. This was accomplished by temporarily detaching the lateral rectus, freeing the adhesions between the two muscle sheaths and advancing the inferior oblique along the sclera in its line of action (fig. 8A). When anatomic considerations precluded advancement to the degree desired, a small resection was added at the tip. Buried sutures of chromic surgical gut, silk or nylon were used to anchor the muscle to the sclera. It was found that a narrow-bladed hemostat was a more satisfactory muscle clamp in this situation than any of the conventional ones. Before the lateral rectus was replaced, a tongue of Tenon's capsule was brought down over the advanced inferior oblique to prevent any possible adhesions between the two muscles (fig. 8B).

This technic has been used in 15 advancements of 15 paretic inferior oblique muscles in 11 patients.

#### RESULTS AND ILLUSTRATIVE CASES

As in the case of tucking of the superior oblique muscle, no obvious relation was found between the number of millimeters of advancement

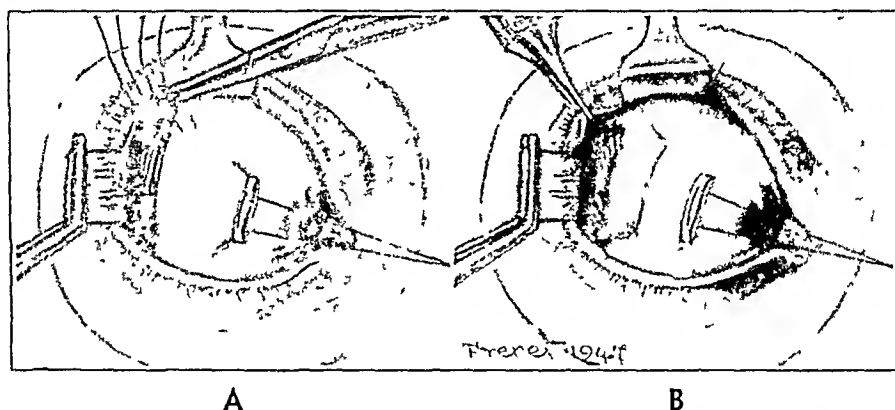


Fig. 8.—A, advancement of inferior oblique under lateral rectus muscle; B, Tenon's capsule flap over advanced inferior oblique and under lateral rectus.

and the number of prism diopters gained. Three cases illustrating different situations in which this operation was useful follow.

#### CASE 6.—*Congenital Paresis of the Inferior Oblique with Secondary Convergent Strabismus.*

J. D., an 11 year old boy, was referred on Aug. 8, 1945 for operation on a congenitally paretic inferior oblique muscle in the right eye. His mother stated that he was "born with a turned eye." On examination he was found to have marked weakness of the inferior oblique muscle of his right eye and convergent strabismus. Vision was 20/20 in each eye, and fixation alternated. When he fixed with the right (paretic) eye, a marked vertical deviation developed. When he fixed with the left (nonparetic) eye, there was a pronounced right convergence. Except for the motor anomaly (fig. 9) the eyes were normal. Measurements by screening gave the following values:

ST 55△

ST 50△ LH 18△

ST' 60△ LH' 18△

ST 60△

RH-LH

ST 60△

LH 45△

ST 60△

LH 20△

On Sept. 27, 1945, with the patient under ether anesthesia, 5 mm. was resected from the tip of the right inferior oblique, and the new end was advanced 11 mm. along the sclera and a Tenon's capsule apron drawn over this muscle, as shown in figure 8. A resection of 8 mm. was done on the right lateral rectus as it was replaced. This surgical procedure on the lateral muscle was not expected to be adequate, but the rest of the correction was reserved for a second stage.

The postoperative course was uneventful, leaving some undercorrection both vertically and horizontally, as follows:

ST 40△		ST 40△
RH 4 △		LH 18△
	ST 40△ LH 14△	
	ST' 45△ LH' 18△	
ST 40△		ST 40△
RH Trace		LH 10△

On Feb. 21, 1946 the second operation was performed, with the patient under ether anesthesia. Recessions of 2.5 mm. were performed on both medial rectus muscles and recession of 4 mm. was done on the left superior rectus muscle. This procedure resulted in a fairly satisfactory result, with good, but not

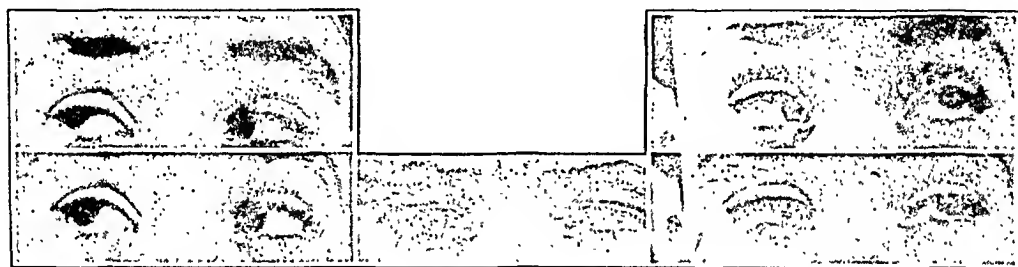


Fig. 9 (case 6).—Congenital paresis of right inferior oblique (preoperative appearance).

perfect, elevation in the field of the right inferior oblique (fig. 10). The most recent muscle measurements, on Dec. 17, 1947, were:

RH 2△	S 8△ LH 3△	LH 8△
	S' 8△ LH' Trace	
RH 3△		LH 4△

No further surgical correction is indicated.

#### CASE 7.—Paresis of Both Inferior Oblique Muscles in Convergent Strabismus.

B. B., 6 years old, a surgeon's daughter, was brought in by her father, who stated that her eyes had been "out of line" both horizontally and vertically all her life. She was otherwise a normal, healthy girl. Examination disclosed vision of 20/20 in each eye and globes that were normal except for the motor function. There was obvious underaction of the lateral rectus and the inferior oblique muscles of both eyes.

Measurements of muscle balance were:

ST 40△		ST 47△
RH 20△		LH 16△
	ST 40△ LH 6△	
	ST' 30△ RH' 4△	
ST 30△		ST 28△
RH 12△		LH 7 △

On Dec. 6, 1945, with the patient under ether anesthesia, the inferior oblique muscles were advanced (10 mm. for the right eye and 12 mm. for the left eye),

and the lateral rectus muscles were resected (8 mm. for the right eye and 10 mm. for the left eye). After a mild postoperative reaction, the eyes settled down to normal function and position. The most recent measurements, on Oct. 21, 1947, showed a trace of exophoria in the primary position and orthophoria in the fields (fig. 11).

CASE 8.—*Paresis of the Inferior Oblique as Part of "Double Elevator Palsy."*

J. M., a 7 year old girl, was referred from another hospital for surgical treatment of "double elevator palsy." The parents complained that the eyes had "never focused" and that most of the time one was closed.

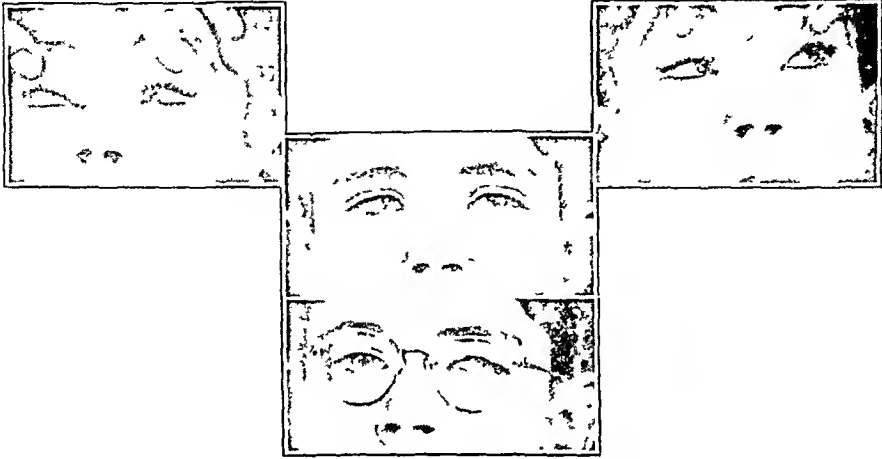


Fig. 10 (case 6).—Function of right inferior oblique improved by advancement of the insertion



Fig. 11 (case 7).—Function of both inferior oblique muscles restored by advancement.

On examination she was found to have pseudoptosis and partial amblyopia (20/70) in the right eye. The left eye had normal (20/20) vision. When she fixed with the left eye, the right lid drooped to occlude vision in the slightly depressed and adducted right eye (lowest photograph, fig. 12). When she fixed with the right eye, the lid opened and the left eye turned up and in (center

photograph, fig. 12). On attempts to look up, the right eye failed in all fields (upper photographs, fig. 12). Measurements of muscle balance were:

LH 80△  
ST 50△

LH 45△  
ST 50△

LH 50△ (right fixation)  
LH 30△ (left fixation)  
ST 50△

LH 40△  
ST 60△

LH 40△  
ST 55△

She had obvious paresis of both elevator muscles of the right eye with secondary pseudoptosis and convergent strabismus. Since fixation was made with the left eye in all fields, the theoretically proper approach would be to the right superior rectus and right inferior oblique muscles. However, it was felt that adequate correction could not be achieved with these muscles alone, and the left elevator muscles should also be weakened. On March 28, 1946, with the patient under ether anesthesia, the right inferior oblique was resected 4 mm. and the tip advanced



Fig. 12. (case 8).—Double palsy of the elevator muscles (preoperative appearance).

14 mm., the right superior rectus resected 6 mm., the right lateral rectus resected 10 mm., the left inferior oblique receded 9 mm. and the left superior rectus receded 3 mm., in one operation. The immediate postoperative reaction was moderately severe. On the fifth postoperative day measles developed, and the course of convalescence was stormy. By May 3 (two months after operation) the eyes were quiet and well healed, with considerable improvement. Measurements of muscle balance at that time were:

LH 9 △  
ST 12△

LH 8△

ST 5 △ LH 3△  
ST' 12△ LH' 3△

LH Trace  
ST 8△

LH Trace

Some pseudoptosis remained. The child disappeared from observation after that time, and all attempts at follow-up have been unsuccessful. Final measurements and postoperative photographs have not been obtained.

## COMMENT

The technics described in a previous section, and illustrated in figures 2 and 8 have proved highly satisfactory in direct surgical strengthening of paretic oblique muscles. Certain factors which experience with these operations has shown deserve comment.

These methods, although they are technically somewhat more difficult than the commoner operations of the rectus muscles, are entirely practicable. If they are performed neatly and without unnecessary trauma to tissues, they do not cause much more reaction than do the conventional muscle operations. They therefore add to our surgical armamentarium procedures which make it possible to plan and effect

TABLE 1.—*Correction Obtained by Tucking the Superior Oblique Muscle*

Tuck, Mm.	Correction Obtained					
	Distant Vision		Near Vision		Field	
	$\Delta$	$\Delta$ /Mm.	$\Delta$	$\Delta$ /Mm.	$\Delta$	$\Delta$ /Mm.
12	12	1.0	14	1.2	41	3.4
10	3	0.3	4	0.4	10	1.0
10	9	0.9	11	1.1	22	2.2
12	.	...	..	...	12	1.0
10	1	0.1	3	0.3	12	1.2
8	4	0.5	5	0.6	12	1.5
12	13	0.8	10	0.8	18	1.5
10	7	0.7	7	0.7	10	1.0
12	10	0.8	12	1.0	21	1.8
10	14	1.4	14	1.4	21	2.1
10	6	0.6	6	0.6	19	1.9
16	36	2.3	..	...	32	2.0
14	12	0.9	12	0.9	38	2.7
8	2	0.3	3	0.4	14	1.3
15	25	1.7	26	1.7	..	...
20	25	1.3	30	1.5	..	...
18	10	0.6	14	0.8	40	2.2
8	2	0.3	4	0.5	12	1.5

correction in the more complicated muscle cases according to the best accepted principles. Undesirable compromises are less often necessary, and better functional results can be obtained.

The greatest difficulty in these operations is the necessity of judging the amount of correction to be made by the appearance and feel of the muscle at operation. Perhaps this difficulty is to be expected, for it is well known that exact surgical correction of even the simple horizontal deviations cannot be exactly calculated in advance but must be modified after the muscle is exposed. In spite of this difficulty, results well within acceptable limits<sup>14</sup> can be obtained. Analysis of the number of prism diopters gained in the primary position and in the field of

14. Dunnington, J. H., and Wheeler, M. C.: Tr. Am. Acad. Ophth. 46:206, 1941.

action of the muscle for each millimeter of surgical correction are shown in table 1 for the superior oblique muscle and in table 2 for the inferior oblique muscle. It can be seen that variation is wide both in tucking of the superior oblique and in advancement of the inferior oblique. An average of the results obtained yields a figure of nearly  $1\Delta$  gain per millimeter of muscle correction, and to be expected in the primary position of nearly  $2\Delta$  in the field of action of the muscle. However, the individual variations are wide.

The figures are practically the same for tucking of the superior oblique and advancement of the inferior oblique muscle. There seems to be a correlation between the appearance of the muscle or tendon and the amount required, but there is no way to express this mathematically. There appears to be no way by which to judge the amount

TABLE 2.—*Results of Advancement\* of the Inferior Oblique*

Advancement, Mm.	Correction Obtained					
	Distant Vision		Near Vision		Field	
	$\Delta$	$\Delta$ /Mm.	$\Delta$	$\Delta$ /Mm.	$\Delta$	$\Delta$ /Mm.
16	4	0.3	0	0	27	1.7
10	6	0.6	..	...	16	1.6
12	..	...	4	0.3	20	1.6
14	13	0.9	18	1.3	47	3.4
10	2	0.2	1	0.1	4	0.4
13	10	0.8	12	0.9	27	2.1
11	16	1.5	16	1.5	24	2.2

\* The other inferior oblique operations were sufficiently complicated by additional surgical correction of the vertical muscles that the exact amount attributable to individual operations on the oblique muscles could not be accurately estimated.

of surgical correction required better than that of adjusting the tension according to the surgeon's sense of touch.

A word should be added about immediate overcorrection. In all satisfactory cases the appearance in the immediate postoperative period is one of pronounced overcorrection. If this is not present, the final result may be expected to be an undercorrection.

### SUMMARY

The reasons for direct operative procedures to strengthen a weak oblique muscle are cited. Technics for tucking a paretic superior oblique and advancing a paretic inferior oblique muscle are described. Illustrative cases in which the three technics were successfully applied are reported. The methods of judging the amount of operation to be performed are discussed.



# Ophthalmologic Reviews

## AQUEOUS VEINS AND THEIR SIGNIFICANCE FOR PATHOGENESIS OF GLAUCOMA

K. W. ASCHER, M.D.

CINCINNATI

### DETECTION AND QUALITIES OF THE AQUEOUS VEINS

ALL OVER the body, fluid may leave or enter capillaries according to the relative values of tissue pressure and intravascular pressure and osmotic and colloidal osmotic pressure which prevail inside and outside the vessel walls. An individual capillary may yield tissue fluid in its proximal part and accept tissue fluid in its distal part.<sup>1</sup> In the human eye, there is superimposed on this universal water exchange through the capillary endothelium a continuous gross circulation of fluid, with its source in the ciliary body and its goal in the chamber angle.<sup>2</sup> From the angle of the anterior chamber fluid seeps through the trabecular meshwork into the canal of Schlemm, hence through the scleral venous meshwork and, finally, into conjunctival and episcleral veins, where it may become biomicroscopically visible.<sup>3</sup> This circulation of fluid was postulated by Leber<sup>2a</sup> and his followers<sup>4</sup> but was never definitely proved or really observed. For decades, many investigators denied the existence of a continuous production and elimination of fluid into and out of the eye.<sup>5</sup> The detection of the aqueous veins, in 1941,

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The Snyder Ophthalmological Foundation made grants in aid for research on aqueous veins.

1. Best, C., and Taylor, N.: *Physiological Basis of Medical Practice*, ed. 4, Baltimore, Williams & Wilkins Company, 1945, pp. 23-26.

2. (a) Leber, T.: *Die Zirkulation und Ernährungsverhältnisse des Auges*, in Graefe, A., and Saemisch, T.: *Handbuch der gesamten Augenheilkunde*, ed. 2, Leipzig, Wilhelm Engelmann, 1903, vol. 2. (b) Duke-Elder, W. S., and Davson, H.: *The Present Position of the Problem of the Intraocular Fluid and Pressure*, *Brit. J. Ophth.* **32**:555-569 (Sept.) 1948.

3. Ascher, K. W.: *Aqueous Veins: Preliminary Note*, *Am. J. Ophth.* **25**: 31-38 (Jan.) 1942.

4. (a) Seidel, E.: *Mikroskopische Beobachtungen über den Mechanismus des Abflusses aus der Vorderkammer des lebenden Tieres*, *Arch. f. Ophth.* **112**:170 (March) 1923. (b) Serr, H.: *Mechanik der Augendruckschwankungen beim primären Glaukom*, *Ber. ü. d. Versamml. d. deutsch. ophth. Gesellsch.* **45**:225, 1925.

5. Hamburger, C.: *Antwort auf Seidels Aufsatz, zum Beweis der Filtrations Theorie*, *Klin. Monatsbl. f. Augenh.* **72**:206, 1924. Weiss, O.: *Physiologie der*

*(Footnote continued on next page)*

disproved the assumption of stagnation of the intraocular fluid. With a continuous flow of intraocular fluid leaving the canal of Schlemm through the aqueous veins, a continuous production of aqueous humor is postulated.<sup>6</sup>

Aqueous veins are biomicroscopically visible channels resembling blood vessels and connecting the canal of Schlemm and its outlets into the deep scleral meshwork with the superficially visible conjunctival and episcleral vessels. They can be found in almost every normal human eye<sup>7</sup>; in eyes of experimental animals<sup>8</sup> they can be photographed, although not without difficulty,<sup>9</sup> and repeated photographs have proved that they are stable anatomic features which do not change their location and course after months and years.<sup>10</sup> Larger aqueous veins may be detected by means of a simple magnifying loupe of 10 diameters.<sup>11</sup>

It may seem incredible that these important structures escaped the attention of physiologists and ophthalmologists for decades after the introduction of slit lamp microscopy. This was due to several factors: lack of interest in studying the limbal region of normal eyes; the small size of many of these aqueous veins when they arise in the limbal meshwork; the blood which often joins the clear fluid while streaming through the deep scleral meshwork and after leaving the sclera, and the traditional, but disadvantageous, custom of using only the narrow slit of the corneal microscope. According to a drawing published in 1934, Graves<sup>12</sup> probably saw an aqueous vein, and so possibly did

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Ernährung und der Zirkulation des Auges, in Schieck, F., and Brückner, A.: *Kurzes Handbuch der Ophthalmologie*, Berlin, Julius Springer, 1932, vol. 2. Magitot, A.: *Le liquide endoculaire et la nutrition du globe*, in Bailliart, P.; Coutela, C.; Douglas, N., and Bucy, P. C.: *Traité d'ophtalmologie*, Paris, Masson & Cie, 1938, vol. 2. Fischer, F. P.: *Der Wasserhaushalt des Auges und seiner Teile*, *Docum. ophth.* **1**:79-160, 1938.

6. Ascher, K. W.: Physiologic Importance of the Visible Elimination of Intraocular Fluid, *Am. J. Ophth.* **25**:1174-1209 (Oct.) 1942.

7. de Vries, S.: *De zichtbare afvoer van het kamerwater*, Amsterdam, Drukkerij Kinsbergen, 1947.

8. Schmerl, E.: Significance of Action of Paredrine on the Ocular Tension of Rabbits, *Am. J. Ophth.* **30**:186-190 (Feb.) 1947.

9. (a) de Vries.<sup>7</sup> (b) Gartner, S.: Blood Vessels of the Conjunctiva, *Arch. Ophth.* **32**:464-476 (Dec.) 1944.

10. Ascher, K. W.: Search for Aqueous Veins, *Am. J. Ophth.* **31**:105-106 (Jan.) 1948.

11. Ascher, K. W.: Further Observations on Aqueous Veins, *Am. J. Ophth.* **29**:1373-1387 (Nov.) 1946.

12. Graves B.: Certain Clinical Features of the Normal Limbus. *Brit. J. Ophth.* **18**:305-368 (June) 1934.

others before and after him, without paying due attention to these features. Broad aqueous veins, arising from a scleral emissary, are more easily visible; but most of them are much smaller, and, according to de Vries,<sup>7</sup> the search for them can be compared to the search for the needle in the haystack.

From Theobald's<sup>13</sup> diagrams of the outlets of Schlemm canals, it is evident that the widest outlets were located near the horizontal meridian of all 3 eyes investigated; this region corresponded to the origin of the majority of the aqueous veins.<sup>6</sup> Arising from the limbal meshwork as narrow capillary vessels, or from the depths of the scleral tissue with a slightly wider figure 6-like or U arch, or as wide channels from a scleral emissary, aqueous veins take a rather straight course through the conjunctival or the subconjunctival tissue. They are to be recognized by their pale or limpid coloration, which may vary during the observation and, in many instances, by a layering, consisting of two, three or more strata of differently shaded fluids, the layers running parallel to each other and to the wall of the vessel. The length of an aqueous vein varies from a fraction of a millimeter to 1 cm. or slightly more; what appears to be an unusually long aqueous vein is often a recipient vessel. The width of aqueous veins is between 0.01 and 0.1 mm. Below the point of their emptying into the regular conjunctival or episcleral veins, their clear contents are visible within the recipient vessel for a variable distance, as when a clear creek empties into a muddy river (fig. 1). If a large aqueous vein is found in one eye, a similar one may be detected in the fellow eye symmetrically located.<sup>14</sup> The eyes of parents and children may show aqueous veins at similar locations and with a similar course and qualities.<sup>6</sup>

Stratified currents are not a unique finding; they may be observed in various other organs, as in the tongue and the web of the frog,<sup>15</sup> in the mesentery and the spleen of the mouse<sup>16</sup> and occasionally inside the human eye of the canal of Schlemm when viewed gonioscopically.<sup>17</sup> The same picture may be due to a partition of the canal, however.

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13. Dvorak-Theobald, G.: Schlemm's Canal: Its Anastomoses and Anatomic Relations, *Tr. Am. Ophth. Soc.* **32**:593, 1934; unpublished recent data.

14. Ascher.<sup>6</sup> de Vries.<sup>7</sup>

15. Thoma, R.: Experimentell-mathematische Behandlung des Blutkreislaufs, in Abderhalden, E.: *Handbuch der biologischen Arbeitsmethoden*, Berlin, Urban & Schwarzenberg, 1927, vol. 2, pt. 5, sec. 4, chap. 2, p. 1118, Jaeger, A.: Anordnung und Stellung der rothen Blutkörperchen im strömenden Blut, *Arch. f. d. ges. Physiol.* **235**:715, 1935; *Arch. f. Augenh.* **110**:148, 1937.

16. Kniseley, M. H.: Microscopic Observations of the Circulatory System of Living Unstimulated Mammalian Spleens, *Anat. Rec.* **65**:25 (April) 1936.

17. Troncoso, M. U.: Gonioscopy and Its Clinical Applications, *Am. J. Ophth.* **8**:433-449 (June) 1925.

Embryologically, anatomically and physiologically, the canal of Schlemm, the scleral meshwork and the aqueous veins form a biologic unit charged with the elimination of intraocular fluid.<sup>6</sup> According to computations by various authors, an average of 5 cu. mm. of fluid is eliminated each minute from the anterior chamber via the canal of Schlemm<sup>18</sup>; considering the diameters of the aqueous veins and the speed of the fluid passing these channels, one may arrive at similar figures for the amount of fluid leaving the eye through the aqueous veins.<sup>14</sup> Goldmann<sup>19</sup> reported on experiments which he performed to prove that the contents of the aqueous veins is really aqueous humor.

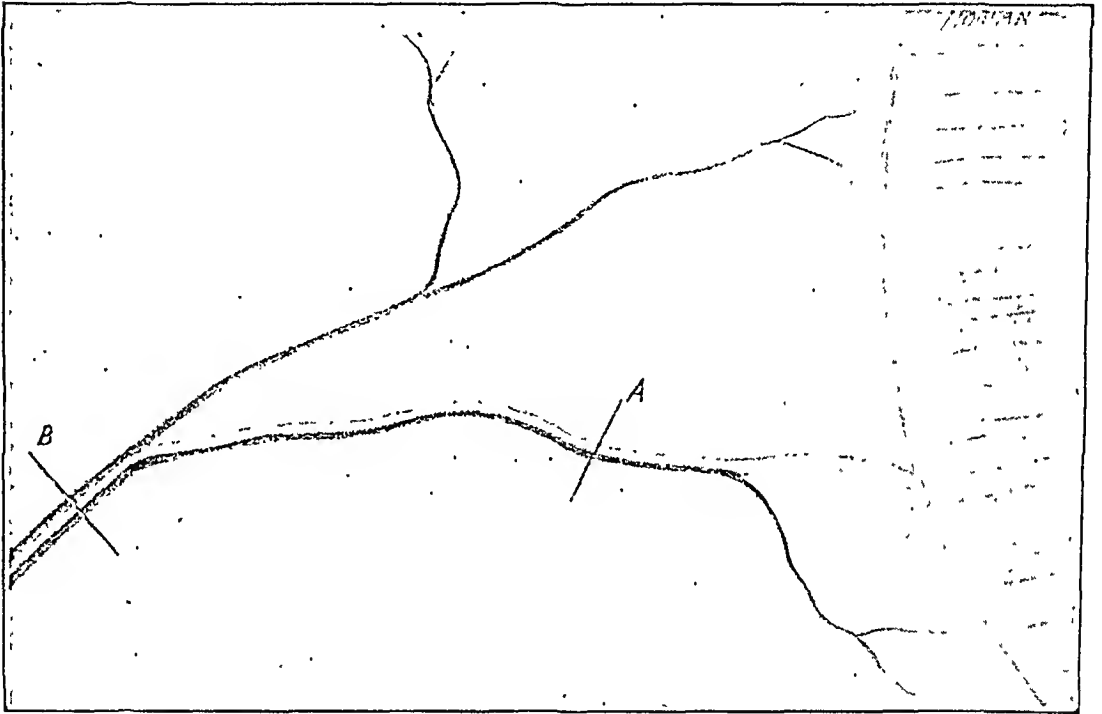


Fig. 1.—Origin and course of a typical aqueous vein (left eye of a white man aged, 48). An aqueous vein starts from the lower nasal portion of the limbus with an arclike origin and empties into a regular conjunctival vein. Below the junction, two strata are visible (A), the clear one being the aqueous section of the recipient vessel. After joining another vein (B), the recipient vessel contains two peripheral red layers and one central aqueous stream (Ascher,<sup>3</sup> page 33).

Physiologic and physical factors, such as heart action, respiration and illumination, have a characteristic influence on the contents of the aqueous veins; illumination enhances the elimination of fluid in many, but not in all, these veins, while pressure of the lids interferes with it in practically every aqueous vein.<sup>6</sup>

18. Duke-Elder, W. S.: *Text-Book of Ophthalmology*, London, Harry Kimpton, 1932, vol. 1, p. 456. Kinsey, V. E.; Grant, W. M., and Cogan, D. G.: *Water Movement in the Eye*, *Arch. Ophth.* **27**:242-252 (Feb.) 1942.

19. Goldmann, H.: *Weitere Mitteilung über den Abfluss des Kammerwassers*, *Ophthalmologica* **112**:344-349 (Dec.) 1946.

Epinephrine reduces, and ethyl morphine hydrochloride increases, the amount of blood in the aqueous veins and in their recipient vessels<sup>20</sup>; homatropine interferes with the elimination of fluid, while physostigmine and pilocarpine increase the output of clear fluid.<sup>21</sup>

#### aqueous veins in glaucomatous eyes

In glaucomatous eyes an increase in clear fluid will appear in the aqueous veins after instillation of pilocarpine.<sup>22</sup> This important fact was photographically recorded by Gartner<sup>9b</sup> in 1944. In congested eyes the aqueous veins become invisible, but they reappear when the congestion subsides; in glaucomatous eyes they may become visible after successful surgical intervention.<sup>22</sup> Periods of increased intraocular pressure coincide with, or may even be preceded by, an increased blood content of the aqueous veins.<sup>23</sup> These minute changes were studied by Thomassen<sup>23a</sup> at hourly intervals.

Sufficient evidence has accumulated since 1941 to prove the presence of a minutely balanced and changeable pressure differential between the two fluids, aqueous humor and blood, flowing in the recipient vessel of an aqueous vein. When, by means of a small cotton applicator, a recipient vessel is compressed distally from the emptying of an aqueous vein, either expulsion of all blood from the blocked section of the vessel or filling with red blood cells may be observed.<sup>24</sup> When compression is released, the picture reappears as it was prior to either phenomenon. These reactions are apparently due to pressure differences in the sources from which the two fluids, blood and aqueous humor, derive, namely, the deep scleral venous meshwork and the canal of Schlemm. For purely descriptive reasons, the aqueous influx was called<sup>3</sup> the glass rod phenomenon because of the resemblance of the clear

20. (a) Ascher, K. W.: Local Pharmacologic Effects on Aqueous Veins, *Am. J. Ophth.* **25**:1301-1309 (Oct.) 1942. (b) Goldmann, H.: Abfluss des Kammerwassers beim Menschen, *Ophthalmologica* **11**:146-152 (Feb.-March) 1946. (c) de Vries.<sup>7</sup>

21. Ascher.<sup>20a</sup> Gartner.<sup>9b</sup>

22. Ascher, K. W.: Glaucoma and Aqueous Veins, *Am. J. Ophth.* **25**:1309-1315 (Oct.) 1942.

23. Ascher, K. W.: Backflow Phenomena in Aqueous Veins of Normal and of Glaucomatous Eyes, *Am. J. Ophth.* **27**:1074-1089 (Oct.) 1944.

23a. Thomassen, T. L.: On Aqueous Veins, *Acta ophth.* **25**:369-376 (Dec.) 1947.

24. (a) Ascher (footnotes 3, 6, 23 and 11) (b) de Vries.<sup>7</sup> (c) Ascher, K. W., and Spurgeon, W. M.: Compression Tests on Aqueous Veins of Glaucomatous Eyes: Application of Hydrodynamic Principles to the Problem of Intraocular Fluid Elimination, *Am. J. Ophth.* **32**: Part II: pp. 239-251, 1949. (d) Goldmann, H.: Ueber Abflussdruck und Glasstabphänomen, *Ophthalmologica* **116**:195-198 (Oct.-Nov.) 1948.

vessel to a rod of glass; a more unequivocal name, aqueous influx phenomenon,<sup>24c</sup> will be used in the future; the opposite effect will be called the blood influx phenomenon, instead of the original term "negative glass rod phenomenon." Neither represents an incidental or transient quality; whenever the test is repeated, the same response will be found, even after months and years, and is characteristic of the particular vessel. De Vries<sup>7</sup> was the first to make photographic records of the blood influx phenomenon. He made the very important observation that the blood influx phenomenon was found in aqueous veins with low speed of flow, e. g., 1.5 mm. per second, while aqueous veins with a measured velocity of 3.5 or 7.5 mm. per second showed the aqueous influx phenomenon.

One might expect that the high pressure prevailing in the anterior chamber of the glaucomatous eye would be transmitted to the canal of Schlemm and hence into its invisible outlets, as well as into the visible aqueous veins; that therefore the aqueous outflow might be more vigorous in glaucomatous eyes, and that therefore the aqueous influx phenomenon might occur in glaucomatous eyes oftener than in eyes with normal pressure. A similar assumption made Verhoeff<sup>25</sup> ask whether in eyes with wide angle glaucoma the clear stream in the aqueous veins might be longer and wider than in eyes with normal pressure. Neither is this so, nor is the aqueous influx phenomenon the rule in the aqueous veins of glaucomatous eyes.<sup>26</sup> The compression of the recipient vessels in such eyes is almost always followed by blood influx, whereby the venous blood streams in a direction opposite its normal flow, namely, not from but back toward the limbus. One should expect, therefore, that on gonioscopic observation blood would be seen rushing into the canal of Schlemm, as it often does in eyes with normal intraocular pressure. Bangerter and Goldmann,<sup>27</sup> as well as Kronfeld and associates,<sup>28</sup> found, however, that backflow of blood into the canal of glaucomatous eyes is observed only as an exception. This contradictory behavior—backflow of blood toward the canal and failure of blood to enter the canal—can be explained by the assumption of narrowing of the outlets of the canal in glaucomatous eyes.<sup>29</sup> Sclerosis of the trabecular meshwork would explain only the influx of blood into the

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25. Verhoeff, F. H., in discussion on Ascher,<sup>20a</sup> p. 1314.

26. Ascher.<sup>22</sup> de Vries.<sup>7</sup> Goldmann.<sup>24g</sup>

27. Bangerter, A., and Goldmann, H.: *Gonioscopy in Primary Glaucoma and Choice of Operation*, *Ophthalmologica* **102**:321-350 (Dec.) 1941.

28. Kronfeld, P. E.: McGarry, H. T., and Smith, H. E.: *Gonioscopic Study on the Canal of Schlemm*, *Am. J. Ophth.* **25**:1163-1173 (Oct.) 1942.

29. Ascher (footnotes 11 and 23). Ascher and Spurgeon.<sup>24f</sup>

blocked recipient vessel and into the aqueous vein, but with a low pressure inside the canal there would be no reason that blood should not stream back into it, as it does in eyes with normal pressure.

Another series of observations gave confirmation of the assumption that at least in some glaucomatous eyes the outlets of the canal of Schlemm are narrower than in eyes with normal pressure: pressure applied to the eyeball externally, and far from any visible aqueous vein, may increase the clear stream in aqueous veins and in recipient vessels.<sup>6</sup> This effect of increase in pressure, which I observed prior to 1942, was carefully studied by Goldmann<sup>30</sup> in Berne and by de Vries,<sup>7</sup> in Amsterdam, in 1946. Using a spring balance, Goldmann measured the amount of external pressure which was needed to widen the diameter of the clear stream in a recipient vessel. Whereas in normal eyes an average of 8 Gm. of external pressure sufficed for this effect, in glaucomatous eyes decidedly higher values, up to 30 Gm. and more, were necessary. In eyes with normal pressure, however, Goldmann found instances in which similarly high values of pressure increment were required in order that a perceptible increase in the clear contents of the recipient vessels should appear. These values were discarded by Goldmann because of their unusually high range. They were noted in eyes with normal intraocular pressure, in the case both of narrow recipient vessels and of those with an unusually slow current. Thus, the high readings are characteristic not of glaucoma but of narrowness of the particular vessel or, most probably, of its origin deep in the scleral meshwork, as suggested by the slow current. In other words, for eyes with normal pressure both high and low increments in pressure are found, whereas for glaucomatous eyes only high readings are present so long as the ocular pressure is elevated.

Mathieu and Weekers<sup>31</sup> encountered aqueous veins less frequently in eyes subjected to iridencleisis than in normal eyes and in eyes with other types of untreated and treated glaucoma. They found aqueous veins in 49 of 50 eyes with normal pressure; a similar ratio was obtained for eyes observed after cataract operation, for eyes with untreated glaucoma and for eyes the pressure of which had been reduced by miotics. Ten eyes subjected to cyclodiathermy several months prior to the investigation showed at least one aqueous vein each. Investigations performed several months, or even years, after iridencleisis showed a ratio of 19 eyes with aqueous veins to 14 eyes without aqueous veins.

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30. Goldmann, H.: Studien über den Abflussdruck des Kammerwassers beim Menschen, *Ophthalmologica* 114:81-94 (Aug.) 1947.

31. Mathieu, P., and Weekers, R.: Contribution à l'étude des veines aqueuses, *Bull. Soc. belge d'opt.*, November 1948.

In order to study a larger series of eyes with complete recovery after iridencleisis, Weekers and Weekers<sup>32</sup> pooled their own cases and those observed by François<sup>33</sup> and found, among 106 eyes, 56 with and 46 without aqueous veins, the findings for 4 eyes being listed as questionable.

In discussing the possible causes of the rare occurrence of aqueous veins after iridencleisis, Mathieu and Weekers excluded (1) postoperative hyperemia, because this had subsided long before the examination; (2) scar formation, which could not possibly be responsible for absence of aqueous veins along the whole limbal circumference, and (3) a peculiar thickening and milky appearance of the conjunctiva, which occurred in very few cases. The authors found, however, that the aqueous veins were less frequent in the series of hypotonic eyes (in 18 of 50) than in the series with pressure readings higher than 15 mm. of mercury; in the latter 38 of 56 eyes showed aqueous veins. They concluded that in an eye with hypotony due to iridencleisis the surgically formed channel might carry the bulk of the fluid which leaves such an eye.

*First Histopathologic Confirmation.*—Unintentionally, Focosi<sup>34</sup> offered what might be the first histopathologic confirmation of my assumption that narrowing or obstruction of the canal outlets are connected with, if not the cause of, a certain type of glaucoma. Focosi described the case of a man aged 44 who, a few hours after operation for glaucoma in his right eye, had his first glaucomatous attack in his formerly normal (left) eye. This left eye had, prior to the operation on the other eye, a shallow chamber but normal intraocular pressure, a normal papilla of the optic nerve, normal visual acuity and a normal visual field. The glaucomatous attack of the intact eye was controlled by miotics before nightfall. Only a few deep corneal folds were visible during the succeeding days. Eight days after the operation, hemoptysis ended the patient's life. The left globe was embedded in pyroxylin, and histologic examination revealed partial occlusion of the chamber angle. Corresponding to the sealed chamber angle, a part of Schlemm's canal was obliterated, and the uncollapsed part of the canal, for a short distance, was obstructed by an amorphous, probably calcareous, cast. In this area one of the canal outlets contained a similar deposit, which stained deeply with hematoxylin and was granular in appearance. Since

32. Weekers, L., and Weekers, R.: Les fondaments physiopathologiques de l'iridencleisis, *Ophthalmologica*, to be published.

33. François, J.: La gonioscopie, Louvain, Librairie rue Fonteyn, 1948.

34. Focosi, M.: Osservazioni istologiche su di un caso recente di glaucoma acuto, *Boll. d' ocul.* **27**:209-227 (June) 1948.



only one of the outlets was obstructed, Focosi justly refrained from overestimating the significance of this first report of a glaucomatous eye with histologically verified occlusion of an outlet of Schlemm's canal. According to Maggiore<sup>35</sup> and Theobald,<sup>13</sup> there are between twenty and thirty canal outlets in every human eye; the smallest outlets have diameters measuring 5 and 30 microns; the diameters of the largest outlets, however, are 50 and 165 microns. It is reasonable to assume that an outlet with a cross sectional area sixty times as large as a small cross sectional area will be more effective for elimination of fluid. In some eyes, only a few large outlets may carry the main bulk of the

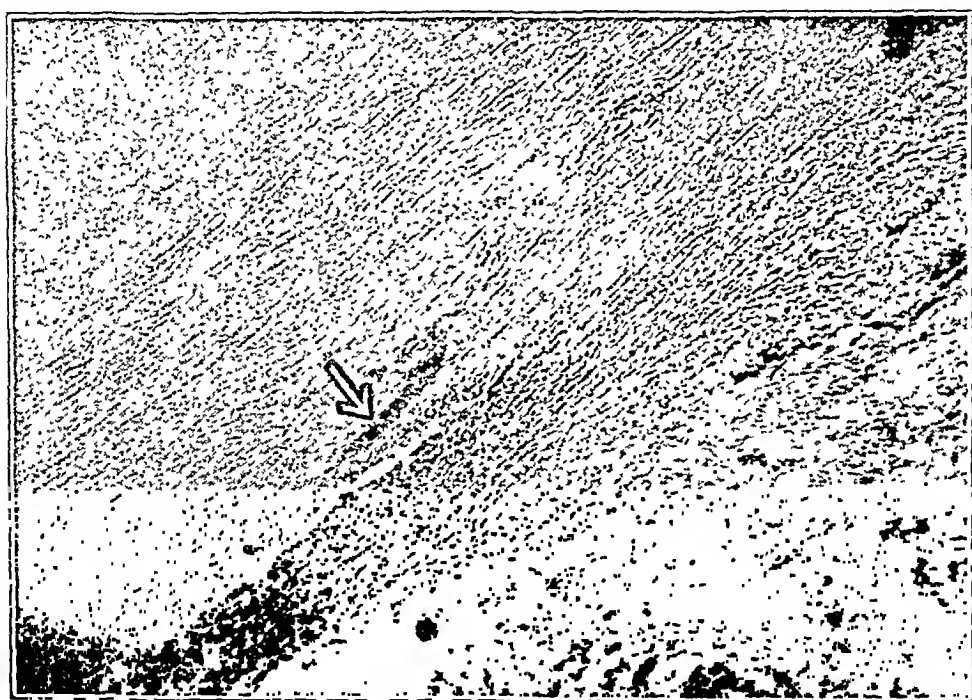


Fig. 2.—Obstruction of canal outlet; histologic confirmation (eye of a man aged 44, who died eight days after his first short glaucomatous attack). The arrow points toward the calcareous cast in the canal outlet (Focosi<sup>34</sup>).

intraocular fluid; occasionally, it may be even one large outlet, as suggested by certain unusually wide aqueous veins, shown in de Vries's photograph no. 33a.<sup>7</sup> In eyes of this type, occlusion of a few, or even of one, outlet may result in marked increase in intraocular pressure. By application of hydrodynamic principles to the problems of elimination of intraocular fluid, these effects can be formulated mathematically.<sup>24c</sup> In Focosi's specimen, the closure of the chamber angle and the collapse of the walls of the canal may have been of greater pathognomonic sig-

35. Maggiore, L.: Struttura, comportamento e significato del canale di Schlemm, *Ann. di oftal.* 40:317-462, 1917.

nificance than the obstruction of one outlet by the calcareous cast; nevertheless, Focosi's observation showed the trend of further research and proved that the expected occlusion of canal outlets may be verified histologically.

#### APPLICATION OF HYDRODYNAMIC PRINCIPLES TO PROBLEMS OF ELIMINATION OF INTRAOCULAR FLUID

Mathematical evaluation by Spurgeon<sup>24c</sup> proved the significance of the diameter of the outlet for the pressure in the outlets and inside the canal of Schlemm. Reduction in the diameter of an outlet from 30 to 20 microns may raise the pressure inside the canal from 16 to 38 mm. of mercury. According to Poiseuille's equation, in which the diameter of the outlet is expressed in the fourth power, a slight reduction in the diameter will be followed by a considerable increase in the pressure at the origin of the outlet.

In addition to a narrowing of the outlets, reduction in their number will, to a mathematically calculable extent, influence the pressure inside the canal of Schlemm. If one half of all outlets are obliterated, say fifteen of thirty, the pressure in the canal, according to Poiseuille's equation, will be raised from 20 to 30 mm. of mercury. Such a reduction in the number of outlets may be expected to occur after a cataract incision unless it is assumed that the severed ends of the outlets can find each other again. Exact suturing of the lips of the wound in proper apposition will increase the chances of reapproximation of the cut ends of the canal outlets—another indication for exact suturing of the cataract incision. Severing of the larger outlets, which are found chiefly near the horizontal meridian, will endanger the eye more than that of smaller outlets.

I shall not enter into mathematical details, but the fact should be mentioned that most of the canal outlets are not circular but elliptic in cross section<sup>35a</sup> and that, according to the modified Poiseuille equation, a greater increase in pressure is to be expected for elliptic cross sections than for circular cross sections of the same square area.<sup>36</sup>

#### CONCLUSION AND SUMMARY

The elimination of intraocular fluid can be studied biomicroscopically.

Considered as a unit of clinicopathologic importance, the canal of Schlemm and the aqueous veins show parallel changes in congestion and in inflammation; in primary simple glaucoma, their responses are apparently contradictory so far as blood has a tendency to overwhelm the aqueous humor and to stream back against, but not into, the canal, which

35a. Dvorak-Therbald.<sup>18</sup> Maggiore.<sup>35</sup>

36. Milne-Thomson, L. M.: *Theoretical Hydrodynamics*, London, The Macmillan Company, 1938, pp. 517-519.

in eyes with normal pressure often becomes filled with blood during gonioscopic observation. These apparent contradictions can be explained in at least some cases of glaucoma by the assumption of a narrowing of the canal outlets.

TABLE 1.—*A Unit of Clinical Significance. The Canal of Schlemm, Its Outlets and the Aqueous Veins*

They Show During	Gonioscopic Appearance of the Canal	Biomicroscopic Appearance of the Aqueous Veins
Inflammation and congestion	Blood often enters the canal	Aqueous veins filled with blood; therefore not discernible
Primary simple glaucoma	Blood rarely enters the canal	After compression of the recipient vessel, blood enters the aqueous vein: blood influx phenomenon
Congestive glaucoma	Canal rarely visible	Aqueous veins carry blood from posterior vein
Glaucoma controlled by miotics or operation	Blood may enter the canal	Aqueous veins reappear, clear fluid may expel blood from blocked recipient vessel, aqueous influx phenomenon

TABLE 2.—*Effect of Width of Canal Outlets and of Aqueous Veins*

Effect on	Wide Outlets	Narrow Outlets
Gonioscopic Findings		
Backflow of blood into the canal of Schlemm	Frequent	Rare
Biomicroscopic Findings		
(a) Rate of flow of aqueous humor, observed on recipient vessel	High	Low
(b) Compression test, performed on recipient vessel, observed on aqueous vein: influx phenomenon	Aqueous influx	Blood influx
(c) Increment pressure test, performed on cornea, observed on recipient vessel: dynamometric readings	Low	High
Intraocular Pressure		
Tonometric readings	Normal if no other pathology	High if many outlets are narrow

No claim is made that this hypothesis can explain all cases of primary simple glaucoma; it is proposed in order to stimulate further research—clinical, histologic and experimental. A large number of new facts have accumulated, and there is, of course, ample space for interpretation; the evidence afforded by gonioscopy and by biomicroscopy is far from complete, and much remains to be done in order that one may approach the problem of glaucoma more satisfactorily. Histologic verification should be supplied for the working hypothesis that a transient or permanent narrowing of the canal outlets seems to be connected with, or even may become responsible for, the increase in pressure in at least some eyes with primary simple wide angle glaucoma. This factor may be purely hypothetic at this time, but it is possible that it plays an important part in setting the scene for the tragedy of glaucoma. As time goes on, one may expect that the aqueous veins will become a source of further light on the problems of physiology and pathology of the intraocular pressure.

# News and Notes

EDITED BY DR. W. L. BENEDICT

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## GENERAL NEWS

**Preresident Training Course, Institute of Ophthalmology.**—The faculty of Columbia University College of Physicians and Surgeons have approved plans to enlarge the preresident training course (formerly given as the basic science course for the residents of the Institute of Ophthalmology and allied hospitals) so that up to 15 applicants who have received or been promised appointments in institutions approved by Columbia University will be accepted for four months' full time training at the Institute of Ophthalmology.

Anatomy, embryology, pathology, physiological optics, bacteriology, pharmacology, physiology, biochemistry and refraction will constitute the basic studies on which further studies preparing the matriculants for training in ophthalmology will be founded. The course will start Jan. 2, 1950. Applications must be submitted before November 1 to the office of the assistant dean in charge of Graduate Medical Education, 630 West One Hundred and Sixty-Eighth Street, New York 32.

**Revised Edition of Motion Picture Reviews Now Available.**—The Committee on Medical Motion Pictures has completed the first revised edition of the booklet entitled "Reviews of Medical Motion Pictures." It now contains all the film reviews published in *The Journal of the American Medical Association* up to Jan. 1, 1949. It also includes a classified table of contents, as well as a list of motion pictures available through the Motion Picture Library of the American Medical Association.

The purpose of the reviews is to provide a brief description and evaluation of motion pictures which are available to the medical profession. Each film is reviewed and commented on by competent authorities.

Copies are available on request from the Committee on Medical Motion Pictures, American Medical Association, 535 North Dearborn Street, Chicago 10.

**Gifts for Medical Library of University of Chile.**—The National Committee for Chile is now receiving gifts for the library of the medical school of the University of Chile at its new collection center in the Library of Congress, Washington, D. C. The newer materials in the library, including periodicals, books and reference materials, were totally destroyed in the recent fire. Medical periodicals of the last ten years and recent medical books are urgently needed. Your contribution will be appreciated.

National Committee for Chile, room 318, Library of Congress, Washington, D. C.

## SOCIETY NEWS

**Pennsylvania Academy of Ophthalmology and Otolaryngology.**—The Pennsylvania Academy of Ophthalmology and Otolaryngology held its annual meeting April 22, 23 and 24 at Harrisburg, Pa.

An interesting program of formal scientific presentations was given, and a round table discussion on "Headache" was presented by specialists in the fields of otolaryngology, ophthalmology, internal medicine and neuropsychiatry.

The following officers of the organization were elected for the ensuing year: president, Dr. Daniel S. DeStio, Pittsburgh; president elect, Dr. Jan G. Linn, Pittsburgh; secretary, Dr. B. F. Souders, M.D., Reading; treasurer, Dr. Bruce A. Grove, M.D., York.

**Joint Meeting of Pan-American Association of Ophthalmology and National Society for Prevention of Blindness.**—A joint meeting of the Pan-American Association of Ophthalmology and the National Society for the Prevention of Blindness will be held March 26 to 30, 1950. This will be the annual meeting of the latter society and an interim meeting of the former. The headquarters of the meeting will be at the Floridian Hotel, Miami Beach, Fla.

## PERSONAL NEWS

**Dr. Brittain Ford Payne to Lecture in México, D.F.**—In México, D.F., August 15 to 27, Dr. Brittain Ford Payne, clinical professor of ophthalmology at New York University Medical College and director of pathology at New York Eye and Ear Infirmary, will give a course of lectures and demonstrations on the histopathology of the eye. During the first week, after a lecture on general considerations and on the stages in the development of the eye, Dr. Payne will discuss in detail the microscopic anatomy of the cornea, sclera and lamina cribrosa (August 16); the choroid, pigment epithelium, retina and optic nerve (August 17), and the ciliary body and iris (August 18). He will close the first week with a lecture on the normal crystalline lens, the zonular fibers, the chambers of the eyeball and the blood vessels and nerves.

Subjects of lectures of the second week will include diseases of the cornea, sclera and anterior segment (August 22); granulomas of the eye, including tuberculosis and sympathetic ophthalmitis (August 23); glaucoma and cataract, and complications following intraocular operations (August 24); traumatic lesions of the eye, including contusions, perforating wounds and intraocular foreign bodies (August 25), intraocular neoplasms and summary (August 26).

## Obituaries

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JOHN GREEN, M.D.

1873-1949

Descended from a notable line of physicians and scientists in England and New England, Dr. John Green gallantly accepted the challenge and became justly distinguished by his own diligence and skill in the practice of ophthalmology and by his devotion to public welfare. An early manifestation of the latter service is recorded by his signature as a founder and subsequent activities in behalf of the Missouri Association for the Blind—now the St. Louis Society for the Blind. His many contributions to ophthalmic literature demonstrated a keen analysis and insight into the intricacies of his chosen field of endeavor, as well as a determination to seek the truth and stand by it regardless of consequences.

A résumé of his professional career, as noted in the *Annual Bulletin* of the St. Louis University School of Medicine, where he served as professor of ophthalmology from 1927 until his untimely death, follows: Bachelor of Arts, Harvard University, 1894; Doctor of Medicine, Washington University, School of Medicine, 1898; instructor in ophthalmology, Washington University, School of Medicine, 1912-1919; associate professor of ophthalmology, St. Louis University School of Medicine, 1922-1926. His annual lectures to the senior class and his conferences with ophthalmic residents were carefully prepared and well received. His hospital services were much more extensive and time consuming than this simple résumé can reveal: intern, St. Louis City Hospital (1898-1899); visiting ophthalmologist, St. Louis Maternity Hospital (1910-1926); associate ophthalmologist, Barnes Hospital (1916-1918) and St. Louis Children's Hospital (1916-1918); ophthalmologist, St. Luke's Hospital (1920-1949), St. Mary's Group of Hospitals (1924-1949), De Paul Hospital (1934-1949); ophthalmologist in chief, St. Louis County Hospital (1935-1949); associate ophthalmologist, St. Louis City Hospital (1924-1926); ophthalmologist (1926-1935); consultant (1935-1949). In addition he found time to give unlimited valuable service as member and officer of the American Board for Ophthalmic Examinations and on the advisory staff of the National Society for the Prevention of Blindness. In both world wars he was a busy member of draft boards. He was co-founder and president of the St. Louis Ophthalmic Society; chairman of the Section on Ophthalmology of the American Medical Association; vice president of the

Missouri State Medical Association, and president of the American Ophthalmological Society—the oldest of its kind in the world—as his father had been in the previous century.

He could not be an indifferent member in any of the numerous organizations that claimed his attention, but it would not be hard to prove that his greatest interest was centered in a home at 243 Westgate, near the western city limits of St. Louis. The intangible treasures of home he bequeaths unsullied to his widow, three sons and three daughters and six grandchildren, who brought him life's greatest charm. Only a great man in mind and soul and body could leave such a record. It was his joy to carry the torch for human progress without weakness until his dying day.

W. H. LUEDDE, M.D.

# Abstracts from Current Literature

EDITED BY DR. WILLIAM ZENTMAYER

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## Anatomy and Embryology

THE RETICULO-ENDOTHELIAL SYSTEM OF THE CORNEA. T. KRZAWICZ, Brit. J. Ophth. 31:421 (July) 1947.

This series of experiments, in which a 1 per cent solution of silver nitrate was applied to the conjunctival sac of rabbits, proves that corneal stroma cells show distinct storing properties for silver, or colloid-opexy, and may in some cases be transformed into typical polyblasts. The opinion that stroma cells correspond to wandering cells in a state of rest seems justified. Corneal stroma cells may thus be classified with elements of the reticuloendothelial system.

The article is illustrated.

W. ZENTMAYER.

## Cornea and Sclera

USE OF ANTI-ALLERGIC DRUGS IN THE TREATMENT OF PHLYCTENULAR OPHTHALMIA. C. F. BOWES, Brit. J. Ophth. 32:163 (March) 1948.

In 15 typical and active cases of phlyctenular ophthalmia, the photophobia, lacrimation, irritation and eczema showed no improvement with diphenhydramine hydrochloride (benadryl®) and 2-(N-phenyl-N-benzylaminomethyl) imidazoline (antistin®), two well recognized anti-allergic drugs. All the patients showed positive reactions in the Mantou tests and roentgen ray evidence of tuberculous infection.

W. ZENTMAYER.

A CASE OF KERATOMALACIA CURED BY PENICILLIN AND VITAMIN A. K. RIZK, Brit. J. Ophth. 32:416 (July) 1948.

The patient, a rachitic, emaciated boy aged 2 years, had had a febrile attack, after which both corneas became opaque. The conjunctivas were dry and showed xerotic spots. There were no signs of inflammation or discharge. The corneas became ectatic and ulcerated. Treatment consisted in the local and general administration of penicillin and a preparation of vitamin A. Vitamin therapy was given in the form of an ointment containing 20 per cent haliver oil and intramuscular injections of a vitamin A preparation ("prepalin"). In five weeks a dense central leukoma covered the pupillary area; the rest of the cornea was clear.

W. ZENTMAYER.

A CASE OF PYOCYANEUS RING ABSCESS OF THE CORNEA TREATED WITH STREPTOMYCIN. J. MASCHLER, Brit. J. Ophth. 32:426 (July) 1948.

The cornea of a boy aged 15 was injured by a splinter of iron. When the patient was seen by the author, on the third day, all but a



1 mm. zone of the periphery of the cornea was infiltrated, the central portion being least involved. A greenish blue hypopyon was present; subconjunctival injections of penicillin into the anterior chamber were used provisionally, and later similar injections of streptomycin were given. On the third day of the use of streptomycin, a Saemisch section was made. Two days later regression set in. A leukoma resulted. Secondary glaucoma supervened, for which an iridectomy was done. The bacterial diagnosis was confirmed by culture. The growth of the bacteria was checked with 500 units of streptomycin.

W. ZENTMAYER.

HISTOLOGICAL ASPECTS OF REFRIGERATED CORNEAL EPITHELIUM. R. SEIDENARI, *Ann. di ottal. e clin. ocul.* 72: 298, 1946.

On the basis of his histologic researches on refrigerated limbal tissue, the author states that the action of cold on the corneal epithelium results in the following phenomena: (1) slight reduction of the total height of the corneal epithelium, (2) slight and somewhat retarded separation of its superficial layers and (3) good and lasting preservation of the turgescence of the basal layer of cells, with excellent preservation of the histochemical properties of the cytoplasm and of the nucleus. Bowman's membrane showed no changes. G. B. BIETTI—J. J. LO-PRESTI.

A CORNEAL TRANSPLANT: HISTOLOGIC EXAMINATION. O. VON FIEANDT, *Acta ophth.* 22: 36, 1944.

A feature of interest in the case reported was the formation of a cyst in the border of the iris. It was considered an implantation cyst, epithelial cells having been introduced by the trephine at the time of the corneal transplantation.

O. P. PERKINS.

### General

THE TEACHING OF OPHTHALMOLOGY. D. VAIL, *Am. J. Ophth.* 31: 535 (May) 1948.

Vail, in this Gradle Lecture, discusses qualifications and facilities for teaching, undergraduate and graduate instruction and residency training and aids to teaching.

W. S. REESE.

MILITARY OPHTHALMOLOGY IN THE EUROPEAN THEATER. D. MARSHALL, *Am. J. Ophth.* 31: 545 (May) 1948.

Marshall recounts the ophthalmologic work of the 298th General Hospital in Bristol, England, at Cherbourg, Normandy, and Liège, Belgium, particularly from the standpoint of military necessity. He also discusses interesting problems and experiences.

W. S. REESE.

### General Diseases

DIABETIC RETINOPATHY. E. REDSLOB, *Ann. d'ocul.* 181: 129 (March) 1948.

The author asks two questions: Is it the life-saving insulin that eventually deprives diabetic patients of their vision, or is the retinopathy

a complication of diabetes which arises independently of the glycosuria and hyperglycemia and escapes the therapeutic action of insulin?

Reference is made to published reports on the incidence of diabetic retinopathy. Despite the fact that the incidence appears to be increasing, the author does not believe that the use of insulin should be discontinued. He does not agree that insulin aggravates the condition.

There is no question that the retinopathy is on a vascular basis—renal, arteriosclerotic or hypertensive. The author believes that insulin has a deleterious effect on the vessels themselves through the intermediary of hypoglycemia. Great care must be taken to insure that hypoglycemia does not occur.

Other factors to be considered are the age of the patient and the duration of the diabetes. The occurrence of arteriosclerosis and hypertension with diabetes is discussed in detail, as well as the possibility of renal damage. The author concludes that the intercapillary glomerulosclerosis which occurs in diabetes is probably responsible for the retinopathy. The renal changes may be present for a long time before there is any evidence of renal damage.

These pathologic changes may in time give rise to hypertension and arteriosclerosis. However, the presence of intercapillary glomerulosclerosis may produce diabetic retinopathy in the absence of any clinical manifestations of hypertension, arteriosclerosis or renal damage. The glomerulosclerosis does not depend on the metabolism of the hydrocarbons as manifested by hyperglycemia and glycosuria. It is probable that diabetes and the glomerulosclerosis have a common origin but that the diabetic retinopathy is not a result of the hyperglycemia.

P. R. McDONALD.

CORNEAL LESION ASSOCIATED WITH DUHRING DISEASE. I. ANGIUS, *Rassegna ital. d'ottal.* 15: 290, 1946.

The author reports a case of Dühring's disease with the typical manifestation on the extensor surfaces of the extremities and a corneal ulcer in the right eye. During the regression of the ulcer a vesicle formed near it, disappearing in four days without rupture; the appearance of the vesicle was accompanied with the formation of numerous bullae in the skin. The corneal lesions disappeared without residual opacity. There was absence of any conjunctival change. Hyposensitivity of the cornea was noted.

This case illustrates that corneal lesions exist early, that the cornea is not always spared of bullae and that pemphigus and shinking of the conjunctiva are two separate entities. The corneal hypersensitivity may indicate a neurotropic origin, already suggested by Dühring as the basis for the dermatitis. The benign course distinguishes it from ocular pemphigus as a separate disease entity.

G. B. BIETTI—J. J. LO-PRESTI.

THE FUNDUS OCULI IN SEVENTY-EIGHT CASES OF CARDIOVASCULAR DISEASE, IN THE AUTOPSY. C. ESPILDORA LUQUE and A. SCHWEITER, *Arch. chilenos de oftal.* 15: 297 (Nov.-Dec.) 1946.

The authors made pathologic studies on 78 subjects who died of various types of renocardiovascular disease and whose eyes had been

examined ophthalmoscopically during life. Twenty-two of the patients were less than 40 years of age. In 7, or 32 per cent, of these young patients the fundus findings were normal. Of the patients over 40 years of age, only 7, or 12 per cent, showed no abnormalities of the fundus. Of the entire series, the fundi were normal in 18 per cent.

The normal appearance of the fundus in both groups of patients was always accompanied with serious lesions of the renocardiovascular system. The renal lesions predominated in the younger group, whereas in the older group the aortic, myocardial, cerebral and renal changes were equally conspicuous.

Usually in the young patients with cardiovascular disease the lesions in the fundus are not pronounced, and a criterion of the general pathologic process and prognosis is not obtained by ophthalmoscopy. An exception occurs in cases of rapidly progressive angionephrosclerosis, in which the changes in the fundus are always severe and pronounced. In spite of the relative normality or slight involvement of the fundus, death in young patients with cardiovascular disease occurs as a result of the serious general involvement.

H. F. CARRASQUILLO.

### Glaucoma

CYCLODIALYSIS: RESULTS. V. SADIKOVA, *Vestnik oftal.* 25: 42, 1946.

An analysis is made of 93 cases (47 of males and 46 of females) in which cyclodialysis was performed; of these, there were 7 cases of compensated and 87 cases of decompensated glaucoma, 2 cases of absolute glaucoma and 2 cases of juvenile glaucoma. The anterior chamber was shallow in 70 cases, moderately shallow in 21 cases and deep in 9 cases. In 43, or nearly half of the cases hyphema was observed during the operation. In most of the cases the blood was absorbed in three to four days; in 12 cases it was absorbed in two weeks. Prolonged presence of blood in the anterior chamber led to an increase of tension in 7 cases. Postoperative iridocyclitis developed in 7 cases. In 1 case the vitreous prolapsed in the wound.

Evaluation of the results of this operation with respect to vision, intraocular pressure and visual fields was as follows: Vision showed improvement in 41 cases and decrease in 13 cases. The intraocular tension was lowered in all but 7 cases. The decrease in tension was gradual. The visual fields were more contracted (from 5 to 20 degrees) after the operation in 12 cases. In 25 cases there was improvement of the visual fields of from 5 to 25 degrees and in 3 cases of 30 degrees.

Thus, the results were encouraging, and Sadikova states the belief that best results are obtained in simple glaucoma in the early stages.

O. SITCHEVSKA.

HOLTH'S IRIDENCLEISIS. P. RIISE, *Acta ophth.* 21: 31, 1944.

The author tabulates his ten years' experience with the iridencleisis operation. A total of 235 eyes, representing glaucoma simplex, secondary glaucoma and acute glaucoma were operated upon. He believes that the operation gives reliable and lasting reduction of tension and few complications.

O. P. PERKINS.

## Injuries

SPONTANEOUS EXPULSION OF NUMEROUS WOODEN FRAGMENTS FROM THE EYE: REPORT OF A CASE. E. BOCHEVER, *Vestnik oftal.* 26: 36, 1947.

The interest of this case is the spontaneous expulsion of several wooden fragments from the eye within a period of two years. A soldier aged 29 was injured by fragments from an exploded mine. The left eye was enucleated at the front line hospital two days after the injury. Six months later, in the hospital, he presented an irritated right eye, with a corneoscleral scar at 9 o'clock and partial cataract and organized vitreous exudate. The roentgenogram showed no intraocular foreign body. However, at intervals of a few months there would appear a bulging at the scar of the sclera or conjunctiva, and on incision one or two wooden fragments could be extracted at a time.

At the end of two years the result was a quiet eye; the cataract had absorbed, the vitreous had cleared and vision was corrected to a fair amount with a cataract lens. Thus the function of the eyeball was preserved despite the numerous traumas during two years.

O. SITCHEVSKA.

## Lens

EXTRACTION OF CATARACT IN THE PRESENCE OF FLUID VITREOUS. D. B. KIRBY, *Am. J. Ophth.* 31: 585 (May) 1948.

Kirby discusses fluid vitreous in cases of cataract, with particular attention to its recognition. He believes that these cataracts should be removed in the capsule and feels that preplaced sutures are unnecessary. He reports 10 cases.

W. S. REESE.

FAMILIAL CATARACT WITH EXTENSIVE PEDIGREE CHART. I. L. JOHNSTONE, *Brit. J. Ophth.* 31: 385 (July) 1947.

The first family studied consisted of 73 persons, 36 males and 37 females. Of the 73, 23 persons, 13 males and 10 females, were affected. The second family consisted of 58 persons, 28 males and 28 females; the sex of 2 was not ascertained.

Distinctive features of the cataract were (a) its presenile onset; (b) its position, primarily posterior, subcapsular, and therefore saucer shaped with concavity directed forward, the cataract thus somewhat resembling cataracta aparathyroidea and ray cataract; (c) its configuration, with leaflike or feather-like branching radiating from the center, so that it somewhat resembled concussion cataract; (d) flakes and dots in white, yellow, green or blue throughout the cortex, but always separated from the anterior capsule by a subcapsular clear zone of disjunction, and (e) the accentuation of the shagreen of the anterior capsule. The earliest signs so far observed were visible only with the slit lamp.

An extensive new pedigree of familial cataract with a mendelian dominant method of inheritance is presented, and the biomicroscopic appearance of the cataract is described. The possibility of other causal

factors is discussed with the help of a review of the relevant literature, and a small series of blood analyses is presented.

The article is illustrated.

W. ZENTMAYER.

### Neurology

CHRONIC SEROUS MENINGITIS. O. PEDICO, *Rassegna ital. d'ottal.* 15: 319, 1946.

The author describes a case of recurrent headache, bilateral papilledema and concentric constriction of the visual field for white and colors. Visual acuity was 20/20 without correction. This spinal fluid showed elevated pressure, was clear and contained 15 cells per cubic millimeter (lymphocytes, 95 per cent; monocytes, 1 per cent, and polymorphonuclear leukocytes, 4 per cent); the albumin measured 0.3 Gm. per hundred cubic centimeters. The author discusses the differential diagnosis and states that the condition in this case was a form of serous endymenitis of Ayala, or chronic serous meningitis.

G. B. BIETTI—J. J. LO-PRESTI.

### Nystagmus

CLINICAL REPORT ON MINERS' NYSTAGMUS. D. A. CAMPBELL, *Brit. J. Ophth.* 32: 193 (April) 1948.

The report is based on the author's observation on 44 patients with miners' nystagmus. Patients with this condition fall into three grades: patients with actual nystagmus, but no symptoms, who continue to work underground; patients who come within the act for certification, who have headache, photophobia or giddiness and who complain that oscillation of lights underground prevents them from working, and patients with psychoneurosis, who, in addition to the usual symptoms, have blepharospasm whenever they are subjected to examination.

The want of treatment and the lack of occupation after certification may easily convert a man of the second category into the third and produce further deterioration in patients of the third grade.

The miner should return to suitable work, e. g., on the surface, as soon as possible—preferably without an interval of unemployment. Fitness for work should be judged by an ophthalmic surgeon and a psychiatrist with special knowledge of the disease.

W. ZENTMAYER.

THE DARK ADAPTATION OF COAL MINERS SUFFERING FROM NYSTAGMUS. F. W. SHARPLEY, *Brit. J. Ophth.* 32: 199 (April) 1948.

Sharpley concludes that the evidence from biochemical tests, although not dramatic, demonstrates that the raised threshold for dark adaptation which is a constant feature among miners, including those with nystagmus, is not due to a lack of vitamin A or D or to any obvious nutritional disturbance.

W. ZENTMAYER.

THE PSYCHIATRIC ASPECT OF MINERS' NYSTAGMUS. E. S. STERN, Brit. J. Ophth. 32:209 (April) 1948.

Stern submits the following recommendation for the management of "miners' nystagmus":

The term miners' nystagmus should no longer be used, but all patients complaining of symptoms which would formerly have been considered under that heading should be referred to a psychiatrist as early as possible for appropriate diagnosis and treatment and should be certified as suffering from the actual psychoneurosis or psychosis found.

All such patients should be found work above ground and in the light, instead of being placed on compensation. This work should be found as soon as possible, though a short period of rehabilitation may be necessary, for psychiatric reasons.

The patients should be under psychiatric supervision.

Lighting in the mines should be improved.

Efforts should be made to ease the posture of the miner at work.

Special attention should be paid to safety measures in the mines.

The miner should be given economic security at his work.

Optimum hours of work in the mines should be worked out scientifically, and this matter should be removed from the sphere of politics.

W. ZENTMAYER.

A COMPARISON OF DARK ADAPTATION WITH THE PSYCHOLOGICAL STATE IN MINERS. D. A. CAMPBELL, Brit. J. Ophth. 32:225 (April) 1948.

According to Campbell, the evidence, such as it is, indicates that among miners there is no significant relation between the psychologic state and the threshold of dark adaptation. It would be interesting to compare miners with a group of ordinary workmen in this respect.

W. ZENTMAYER.

BINOCULAR VISION IN MINERS. D. A. CAMPBELL, R. HARRISON and J. VERTIGEN, Brit. J. Ophth. 32:226 (April) 1948.

The preliminary investigations reported here were made in the hope that a minute study of the behavior of the eyes under conditions of low illumination might reveal the mode of onset of nystagmus.

The binocular vision of miners was compared with that of a large group of normal subjects of the same age groups in full light adaptation and in full dark adaptation (after forty-five minutes in the dark). For subjects able to perform tests for binocular vision, the subjective angle tends to become convergent when they are dark adapted. Miners with nystagmus did not show this phenomenon so strongly. This change did not vary directly with the illumination but appeared to depend on the state of the eye and on the type of visual test. The majority of miners showed an abnormal fixation—their eyes tended to look upward.

The evidence of previous observers is that defective illumination is the primary cause of miners' nystagmus. The authors' observations during the past three years point to a breakdown in binocular vision under conditions of low illumination.

W. ZENTMAYER.

### Ocular Muscles

CONGENITAL ABDUCTION DEFICIENCY. P. MATTEUCCI, *Rassegna ital. d'ottal.* 15: 345, 1946.

After referring to the confusion that still exists with regard to classification, pathology and pathogenesis of congenital abduction, the author reexamines the problem in the light of observations on 3 patients presenting this syndrome, in the special emphasis on the anomalies and malformations frequently associated with the defect.

In the first case, there were enophthalmos of 5 mm., narrowing of the palpebral fissure and paralysis of abduction (20 degrees). Passive motility was possible in every direction. In the second case there were pernicious anemia, ptosis of the right eyelid, paralysis of abduction of the left eye, with an excursion of 2 to 3 mm., and protrusion of the globe and widening of the palpebral fissure. On looking to the right, the left eye retracted 2 to 3 mm., while the palpebral fissure narrowed and the lid drooped; there was no diplopia. The passive motility test showed some difficulty in extreme abduction of the left eye.

In the third case, there were nephrosis, absence of abduction on either side, retraction on adduction and protrusion on attempts at abduction. The patient died of deficient renal function. Postmortem examination did not reveal any anomalies of insertion of the ocular muscle or presence of anomalous muscles, but atrophy of the external rectus muscles was present. Examination of the cranial cavity revealed nothing of significance except for reduction in size of both abducens nerves, reduction of size and in the number of cells and fibers of the nucleus of the sixth nerve bilaterally and no apparent change in the posterior longitudinal fasciculus. After an exhaustive examination of the literature, the author concludes that the cause of the syndrome lies in a lessened capacity of development (aplasia, hypoplasia and dysplasia).

G. B. BIETTI—J. J. LO-PRESTI.

### Operations

AKINESIA. A. KOLEN, *Vestnik oftal.* 26: 39, 1947.

Kolen used the following method of producing akinesia for the past ten years. The injection of 1 to 1.5 cc. of procaine hydrochloride 2 per cent with epinephrine hydrochloride 1:25,000 was begun below the lower margin of the orbital wall 1 to 1.5 cm. temporally to the lateral margin of the orbital wall and continued upward on a vertical line 1 to 1.5 cm. above the upper orbital wall. About 2 cc. of the solution is introduced.

Kolen states that this long vertical line of injection insures full anesthesia of all the branches innervating the palpebral orbicularis muscle and that no edema of the upper lid is encountered, such as occurs in van Lint's akinesia.

O. SITCHEVSKA.

### Orbit, Eyeball and Accessory Sinuses Parasites

THE FAVORABLE ACTION OF ESTRONE IN CERTAIN CASES OF EXOPHTHALMIC GOITER. J. LEDERER, *Am. d'ocul.* 181: 37 (Jan.) 1948.

The author reviews the pathologic physiology of exophthalmic goiter. The production of exophthalmos in animals with preparations of the

anterior lobe of the pituitary is discussed in detail. Clinical and experimental evidence is presented to substantiate the modern concept that the thyrotropic hormone of the pituitary, and not the thyrotoxic hormone of the thyroid, causes the exophthalmos. In some cases the exophthalmos is aggravated by thyroidectomy, and may even be improved by the taking of thyroid. The author was impressed by the number of patients in whom exophthalmic goiter develops at the menopause or after castration.

Five cases of exophthalmic goiter following the menopause or castration are presented in detail. In all cases treatment with estrogenic preparations gave satisfactory amelioration of symptoms and regression of the exophthalmos.

The author believes that the action of the ovarian substances is through the anterior lobe of the pituitary gland. Estrone (folliculin) has an antithyroid action through the intermediary action of the anterior lobe of the pituitary. This checking of the thyrotropic hormone leads to amelioration of the symptoms.

P. R. McDONALD.

### Pharmacology

THE ACTION OF BETAPHENYL-ISOPROPYLAMINE ON THE HUMAN EYE.  
G. SCUDERA, *Rassegna ital. d'ottal.* 15: 94, 1946.

The author conducted experiments on human subjects analogous to those already performed on rabbits in order to study the mydriatic effect of amphetamine in various solutions isotonic with blood. The pupillary diameter obtained with solutions of the drug in sodium nitrate averaged 4.3 mm.; with sodium fluoride, 4 mm., with sodium oxalate and with sucrose, 3.5 mm., and, finally, with sodium and magnesium sulfate, 3 mm.

Mydriasis began in fifteen minutes, was maximum after twenty to forty minutes and disappeared in six to eight hours. No notable irritation, change in tension or change in the caliber of the retinal vessels or of the accommodation was observed.

G. B. BIETTI—J. J. LO-PRESTI.

### The Pupil

VARIATION OF PUPIL SIZE WITH CHANGE IN THE ANGLE AT WHICH THE LIGHT STIMULUS STRIKES THE RETINA. K. H. SPRING and W. S. STILES, *Brit. J. Ophth.* 32: 340 (June) 1948.

Variation in pupillary size depending on the part of the natural pupil through which the light from the external field enters the eye may occur for two reasons: 1. Since the apparent brightness of an illuminated field is reduced when the rays enter near the edge rather than near the center of the pupil (directional sensitivity of the retina), a slightly larger pupil might be expected in the former condition. 2. If, as is possible, the protective action of the constricted pupil consists not so much in reducing the total light flux as in excluding rays which would otherwise strike the retina obliquely, such rays might prove more effective in closing the pupil than would rays of normal incidence. The pupil would then be smaller for rays entering near the edge.



It may be concluded from the present measurements (*a*) that rays entering near the edge of the dilated pupil, and hence incident on the retina at any angle with the normal, do not produce an abnormally high pupillomotor effect and (*b*) that, for practical purposes, the part of the pupil through which light enters the eye is not a factor in determining the size of the pupil.

W. ZENTMAYER.

### Refraction and Accommodation

THE FITTING OF CONTACT LENSES. A. MAGITOT, *Ann. d'ocul.* 180: 430 (July) 1947.

The author describes the various methods employed in the fitting of contact lenses. Patients vary greatly in their tolerance to the wearing of the lenses. Patients with high astigmatic errors or keratoconus frequently wear their lenses for twelve to eighteen hours. There is a small group, about 10 per cent of the patients, who cannot tolerate contact lenses at all. About 80 per cent of all patients who have contact lenses are able to wear them comfortably for several hours.

The author believes that a variation in the amount of tear secretion may account for some of the differences in tolerance. Mention is made of the phenomenon of Sattler. This is a temporary clouding of the cornea that occurs after the lenses have been worn for four to six hours. It disappears rather rapidly. The author believes that it is caused by an abnormality or a deficiency of lacrimal secretion.

P. R. McDONALD.

### Retina and Optic Nerve

THE ALTERATION IN SIZE OF THE NORMAL OPTIC DISK CUP. R. PICKARD, *Brit. J. Ophth.* 32: 355 (June) 1948.

In the present article, 234 eyes observed for fifteen years, or nearly so, are compared with 280 eyes observed contemporaneously with the fifteen year group, but observed only once, and not included in that group. Finally, these two groups are combined, and a general rule as to average growth is deduced. All the disks recorded were normal in appearance. To estimate the size of the cup, a grid was used. The apparent size of the disk and of the cup surface are found, and the size of the cup is expressed as a percentage of the disk. Any cup of a size above 70 per cent should be recorded as suspect and be considered with respect to the visual fields and tension before it can be said to be normal. In 1 eye the cup was 10 per cent smaller at the end of fifteen years. Twelve others showed a decrease at some time, though all these were larger at the end of the fifteen years than at the beginning. One cup was more stationary at the end of the fifteen years than at the beginning. One cup was stationary; it was 36 per cent of the disk. It is not uncommon to have a period of arrest of growth of the cup. Increase in the depth tends to occur with the enlargement of the cup area, but irregularly so. It may be stated as a generalization that if a cup enlarges to 60 per cent of the disk, its depth will increase generally by 0.5 to 1.0 D. A disk may increase to 100 per cent and yet retain a depth of 1.0 D. An increase to 3.0 D. with an increase in the cup percentage

must be investigated by determination of the field and the tension. The possible causes of enlargement of the cup are discussed.

W. ZENTMAYER.

RETINAL ARTERIAL PRESSURE AFTER LUMBAR PUNCTURE. M. MECCA, *Ann. di ottal. e clin. ocul.* 71: 336, 1946.

The author reviews the various theories as to the mechanism by which changes in pressure in the retinal arteries are produced by variations in the intracranial pressure. He reports the results of several studies on the behavior of spinal fluid pressure and intracranial pressure after lumbar puncture. He shows that after lumbar puncture the following changes occur: (1) an immediate rise in the retinal arterial pressure, and (2) a slight drop to the initial level after twenty-four hours. The initial rise is an expression of the shift of intracranial pressure produced by the lumbar puncture, and both these changes, according to the author, are related to a vascular phenomenon.

G. B. BIETTI—J. J. LO-PRESTI.

TWO CASES OF ABLATIO RETINAE CONGENITA NONFALCIFORMIS. H. MOLLER, *Acta ophth.* 23: 353, 1945.

Bilateral detachments of the retina were observed in a boy of 5 years. No tears or other changes were found. One eye was removed because the presence of a malignant growth was suspected. None was found. Later examination of a younger brother, aged 2, showed a similar condition in one eye.

O. P. PERKINS.

### Tumors

CONJUNCTIVAL NEVI. D. ARCURI, *Rassegna ital. d'ottal.* 15: 263, 1946.

The author discusses conjunctival nevi from a clinical standpoint by referring to the literature and by reporting 2 of his own cases. He stresses the importance of slit lamp examination, particularly with respect to the vascularization present. This examination may well be substituted for biopsy, which is technically more difficult and is not free from danger. The stationary nevus should be left undisturbed, while any nevus which increases in size should be freely excised surgically and followed by diathermy coagulation.

G. B. BIETTI—J. J. LO-PRESTI.

CONGENITAL SCLEROCORNEAL CYST: REPORT OF A CASE. V. BISCHLET, *Ophthalmologica* 114: 371 (Oct.-Nov.) 1947.

A case of congenital sclerocorneal cyst is reported. The article is well illustrated. The literature since 1853 is reviewed.

H. P. KIRBER.

### Uvea

A CASE OF RECURRENT APHTHOUS UVEITIS WITH ASSOCIATED ULCUS VULVAE ACUTUM (LIPSCHUTZ). A. RUGG-GUNN, *Brit. J. Ophth.* 31: 396 (July) 1947.

The patient, a married woman aged 22, had had fourteen attacks of the condition, eight in the left eye and six in the right eye. The relapses

were of sudden onset and of relatively short duration. Rigor occurred on several occasions. About eight months after the final attack of uveitis vulval ulceration was noted. There were no dermatologic symptoms. Pregnancy occurred and went on to term. The condition was resistant to penicillin and the sulfonamide compounds.

The evidence seems to point to a virus infection as the most probable explanation of the disease.

The article is illustrated.

W. ZENTMAYER.

CHOROIDAL APOPLEXY DIAGNOSED AS SARCOMA OF THE CHOROID.  
AUW-YANG SIEN, *Ophthalmologica* 115:1 (Jan.) 1948.

The patient, a woman aged 56, had light perception only in the affected eye. The pupil appeared black on transillumination, and no fundus reflex was obtained. The diagnosis was intraocular pigmented tumor, and the eye was enucleated. Histologic examination revealed apoplexy of the choroid, caused by the rupture of a ciliary artery. The author briefly reviews the literature and points out that there is no way of differentiating clinically between hemorrhage and sarcoma of the choroid.

H. P. KIRBER.

### Vision

MONOCULAR OPERATION FOR HIGH DIVERGENT STRABISMUS. L.  
WEEKERS, *Am. J. Ophth.* 31:541 (May) 1948.

Weekers describes an interesting operation for high degrees of divergent squint in which he attaches the internal rectus to the external rectus muscle of the same eye, thus permitting new scleral attachments for the internal rectus. A number of preoperative and postoperative photographs are shown.

W. S. REESE.

SOME ASPECTS OF STUDYING BINOCULAR VISION. K. C. SWAN, *Am. J. Ophth.* 31:845 (July) 1948.

Swan insists on a summary of a patient's deficiencies and analysis of his binocular potentialities as a basis for therapy and evaluation of treatment. He does not consider the patient normal until he demonstrates comfortable single binocular vision under his usual working conditions.

W. S. REESE.

### Visual Tracts and Fields

RECORDING OF VISUAL FIELDS. M. CHAMLIN, *Am. J. Ophth.* 31:565 (May) 1948.

Chamlin describes a method of recording visual fields which permits the examiner to work rapidly, uninterruptedly and accurately.

W. S. REESE.

VALUES AND LIMITS IN COLOR PERIMETRY. G. CRISTINI, *Rassegna ital. d'ottal.* 15:381, 1946.

The author studied a series of patients with diseases of the perceptual and conducting structures in order to collect information on

peripheral color fields. He used (1) chromatic light stimuli (not pigments) of sufficient intensity to obtain a visual field as large as was obtained with white light; (2) light stimuli of equal brilliance and saturation so as to compare the curves obtained, and (3) pure color (monochromatic light). To obtain these stimuli, he used three monochromatic filters from the Leitz photometer placed in front of opal glass and a system of lenses which made parallel rays from a lamp behind the instrument. Photometric determinations were made so as to calibrate the brilliance against changes in the current.

After having reported the limits corresponding to the average values found for 20 normal subjects, the author describes the variations encountered in various ocular disorders: (1) diseases which principally involve the outer layers of the retina (choroiditis, retinitis pigmentosa and detachment of the retina) and inner layers (embolism, thrombosis and glaucoma), and (2) diseases of the conduction apparatus, namely, optic nerve in the region of the chiasm (inflammatory and pressure lesions) and of the geniculocalcarine tract.

A study of the form fields of these patients made at the same time gave following findings: Only in early diseases of the outer layers of the retina was there a disproportion between form fields and color fields, in that amblyopia for blue and green was noted; in diseases of the conducting system, he found no difference between form and color fields so long as the brilliance of the white target and that of the colored target were equal.

The author concludes that the values and the limits of color perimetry in diseases of the conduction system are no different from those obtained by quantitative perimetry.

G. B. BIETTI—J. J. LO-PRESTI.

ANGIOSCOTOMETRY. H. GOLDMAN, *Ophthalmologica* 114: 147 (Sept.) 1947.

The author finds that the breadth of an angioscotoma is dependent on the contrast  $\Delta I/I$ . The angioscotoma becomes wider with diminishing contrast, and always in the direction of the movement of the object. While Evans found that the physiologic angioscotoma increased in a symmetric fashion, with pressure on the eye, pressure on the opposite eye and compression of the jugular vein, Goldman finds that these changes occur, but always in an asymmetric fashion. The angioscotoma increases in breadth in the direction of the movement of the object. This suggests to Goldman that the angioscotoma is not caused by filtration of fluid out of the blood vessels into the surrounding retina, producing a block in conduction, as Evans claimed, but is due to some physiologic property of the retina itself. Further experiments show that other types of scotomas, independent of the retinal vessel tree, show the same characteristics. It is quite apparent, therefore, that the finer so-called angioscotoma is actually a phenomenon of summation, as a result of the rods and cones being connected outside the foveal area with more than one cell station higher up in the synaptic pathway

to the brain. This relationship permits summation and accounts for the appearance and disappearance of the scotoma when the stimulus is subliminal.

F. H. ADLER.

### Vitreous

OX VITREOUS HUMOR: 1. THE RESIDUAL PROTEIN. A. PIRIE, G. SCHMIDT and J. W. WATERS, *Brit. J. Ophth.* 32: 321 (June) 1948.

On the basis of the experimental evidence submitted, the authors conclude that the structure of the vitreous humor of the ox is complex. The vitreous cannot be considered uniform but is made up of at least two "structures," the collagen-like network of the hyaluronic acid and protein jelly. Liquefaction of the vitreous follows enzyme action and is essential for maintenance of a normal vitreous; yet it does not form the vitreous, being minimally swollen at the neutral point and occupying only a very small part of the total volume. It seems that the relation of the network to the jelly is of prime importance and that it must be taken into account in any theory of the causes of swelling and degeneration of the vitreous.

The authors summarize their work as follows: Roentgenology, amino acid chromatography and enzyme analysis provide evidence that the residual protein of the vitreous humor of the ox is largely of collagen type. Enzyme preparations containing collagenase liquefy the ox vitreous. The bearing of this observation on the conception of the structure of the vitreous is discussed.

W. ZENTMAYER.

EXPERIENCES WITH TRANSPLANTATION OF HUMAN VITREOUS. O. VON FIEANDT, *Ophthalmologica* 115: 257 (May) 1948.

Vitreous taken from human eyes from eight hours to three days after death was transplanted into 4 human eyes. Two of these eyes were ultimately lost, owing to a violent inflammatory reaction. The remaining 2 eyes tolerated the foreign material well, 1 of them on two occasions. In 1 eye a detached retina was found to be well in place after the procedure. The blood groups of the donor and recipient seem to have no influence on the outcome of the operation. The intradermal injection of the donor's vitreous (Hobart test) is not a reliable indicator of hypersensitivity.

H. P. KIRBER.

### Therapeutics

ACTION OF PRISCOL® ON THE VESSELS OF THE RETINA. B. MILLER, *Ophthalmologica* 115: 11 (Jan.) 1948.

Priscol® (2-benzyl-4,5-imidazoline hydrochloride) has been used with good results in treatment of caustic burns of the eye, keratitis and iridocyclitis. The drug acts as a vasodilator on the retinal vessels. Patients with retinal arteriolar spasms were selected for the study. Six to 10 intravenous injections of priscol® 0.01 Gm., were given over a period of fourteen days. Subjective improvement consisted of decrease in fatigue and headaches; objective improvement was evident in widening of the retinal arteries, decrease of blood pressure, and better visual

acuity. The drug acts as a dilator on spastic, as well as on normal, arteries. Measurements were made with the Lobeck method on 10 normal subjects and on 10 subjects with arterial spasm. The results are tabulated. Two cases are described in detail. The first patient, a man aged 66, had thrombosis of a branch of the upper temporal vein in one eye. He also presented moderate congestion of the lungs, acrocyanosis and insufficiency of the coronary vessels. After three weeks of treatment with priscol,<sup>®</sup> his vision improved from 2/35 to 5/20, and the fields also showed decided improvement. The second patient, a man aged 66 with diabetes and chronic nephritis, showed only moderate improvement of visual acuity and fields but experienced marked subjective improvement in general.

H. P. KIRBER.

# Society Transactions

EDITED BY DR. W. L. BENEDICT

## OXFORD OPHTHALMOLOGICAL CONGRESS

H. B. Stallard, M.B.

*Thirty-Third Annual Congress, July 3, 4 and 5, 1947, London*

The Thirty-Third Annual Oxford Ophthalmological Congress was held July 3, 4 and 5, 1947.

The Doyne Memorial Lecture was admirably delivered by Dr. Leon Stansfield Stone, Bronson Professor of Comparative Anatomy, Yale University, on the subject "*Return of Vision and Functional Polarization in Retinas of Transplanted Eyes.*"

Salamander eyes offer unique opportunities for developmental and regenerative studies of the retina and optic nerve fibers. Long before the sensory layers in the retina are even differentiated it is possible to uncover the moment at which the future functional patterns in the retina are determined. This is borne out by the observation that when the embryonic eye is rotated 180 degrees subsequent to the late tail bud stages the visuomotor responses are completely reversed in the larval and adult life of these hosts. A similar operation earlier than this period in development is followed only by normal vision.

Although the retina survives in transplanted larval eyes, it degenerates and then regenerates in adult grafts. After transplantation in the adult eye the functional patterns in the retinal quadrants can be made to reestablish themselves in the new retina. Vision can return four times in the same adult salamander eye repeatedly transplanted to a new host. The eye can also be successfully transplanted after seven days of refrigeration.

Normal visuomotor responses are easily demonstrated as the animal follows a lure approaching in all directions. The animal also automatically follows vertical black and white stripes in a drum rotating in one direction only (temporonasally) through the field of vision of an eye (clockwise for a left eye; counterclockwise for a right eye).

If the grafted eye is normally oriented, visuomotor responses are normal. If the excised eye is reimplanted upside down (all retinal quadrants rotated 180 degrees), abnormal swimming reactions and reversed visuomotor responses are established after the new retina and optic nerve regenerate. The effect is the same as in the control experiment, in which the normal eye is rotated 180 degrees in situ, with preservation of the original retina and nerve. In either case normal vision is restored immediately by rotating the eyes in situ back to normal position without injury to the retina or nerve.

The dorsoventral and nasotemporal axes may be independently rotated 180 degrees in a single eye by exchanging the right and the left eye and properly orienting them. Only through the reversed retinal quadrants are the visuomotor responses reversed. Rotated eyes grafted to animals of different species give similar results. The abnormal visuo-

motor responses have remained established in animals kept alive for three and one-half years. The application of these studies to visual acuity and color vision was discussed, and a colored motion picture, illustrating with beautiful precision the results of these investigations, was shown.

This excellent lecture was immensely appreciated by the large audience present.

The discussion on "The Contracted Socket" was opened by Prof. T. Pomfret Kilner and Mr. H. B. Stallard. Professor Kilner discussed the causes of contraction and commented on the suddenness with which this occurred in some cases. He expressed himself in favor of using a very thin skin graft (Thiersch). He showed a variety of operative prostheses intended to produce overcorrection and to allow for subsequent contraction of the socket. Retention of these "forms" was by central tarsorrhaphy. Professor Kilner discussed the treatment of unpleasant odor from skin graft sockets by swabbing with "cetavlon" (cetyl trimethyl ammonium bromide) and grease massage. He showed lantern slides of treated cases and a cinema of the standard technic used in his clinic at Roehampton.

Mr. Stallard described the anatomic requirements of the ideal socket and the common defects and deformities seen in contracted sockets. He discussed the mechanical enlargement of some contracted sockets by graduated sizes of acrylic molds, held, if necessary, by a retention device consisting of a screw bolt buried in an acrylic mold and attached by three pins and two universal joints to a plate buried in a plaster of paris head band.

He described his technic of conserving palpebral conjunctiva and using full thickness skin grafts cut to a special pattern to fit the concave under surface of an acrylic mold, which was shaped to the ideal size of the prosthesis ultimately required for the patient. The acrylic mold was perforated with two central holes 3 mm. in diameter for the escape of discharges from the socket. The free skin graft was sutured to the edges of the conjunctiva in the upper and lower fornices and at the medial and lateral canthi.

To date, such grafts had taken completely; a good projecting mound was formed in the socket floor to fill the concavity of the ultimate prosthesis; there had been no foul discharge or smell and no obvious contraction of the graft. It was stated that such work was still in the experimental stage and that it was too early to make a definite recommendation for the acceptance of this technic. The results showed, however, that the marriage of skin and conjunctiva was not always an unhappy one.

Mr. Stallard commented that the full thickness graft was tried because the Thiersch grafts always underwent considerable contraction.

Miss Savory (London), in her paper entitled "Uses of Thrombin and Fibrinogen in Ophthalmic Surgery," spoke of the importance of using higher concentrations of fibrinogen and thrombin than are normally present in the blood in order to produce firmer and quicker clotting. Human fibrinogen is used in a 1.5 per cent solution (the normal fibrinogen content of the blood is 0.25 per cent), and thrombin in a concentration of 5 units per milliliter. First, the graft bed and the deep surface of pedicle grafts are flooded with fibrinogen, and later 2 or 3



drops of thrombin are added. The graft is spread into its proper position at once.

In the case of free mucous membrane and epidermal grafts applied to the eye and socket, sutures are necessary, and these are placed before fibrinogen and thrombin are applied, through a lacrimal cannula inserted beneath the graft.

These substances are not satisfactory for conjunctival flaps reflected in the surgical repair of squint and retinal detachment, but are effective in sealing conjunctival flaps in the classic cataract extraction operation and the torn edges of lacerated wounds of the conjunctiva.

The fibrin clot, tinted with methylene blue, is also used in distending the lacrimal sac for excisions. Thrombin, 5 units per cubic centimeter, has been injected into the anterior chamber to prevent hyphema in cases of new vessel formation on the iris and to wash out the anterior chamber after evacuation of the blood in cases of recurrent hyphema.

Mr. Tudor Thomas described his technic of obtaining by a trephine donor corneal grafts from cadavers, leaving the rest of the eye in situ.

Mr. George Black gave an account of the diagnostic value of injecting methylene blue, 3 minims (0.18 cc.) of a 0.1 per cent solution, beneath the retina. The sclera is trephined at the site for injection. The detached area of the retina rapidly stains and tears show up vividly as red patches against the blue background. The choroid does not stain.

At the end of the Congress, an excellent and most interesting cinema and demonstration was given of Dr. Norman L. Cutler's operation, a ball and ring implant into Tenon's capsule after excision of the eye.

## NEW YORK ACADEMY OF MEDICINE, SECTION OF OPHTHALMOLOGY

*Brittain F. Payne, M.D., Chairman*

*Milton L. Berliner, M.D., Secretary*

*May 19, 1947*

### INSTRUCTION HOUR

**Common Errors in Fitting Glasses.** MR. AUREL MANGOLD (by invitation).

**Aids to Subnormal Vision.** MR. CONRAD CARLSON (by invitation).

**Plastic Eye Exhibit.** MAJOR STEPHEN F. SMOLCZYNSKI, D. C., United States Army (by invitation).

### PAPERS OF THE EVENING

**Heredoretinal Degenerations Associated with Brucellosis.** DR. EDWIN M. BURTON (by invitation).

Cases of macular degeneration of the adult type occurring in 2 brothers and 1 sister were reported. Each patient gave strongly positive reactions to tests for brucellosis. There was no history of consanguinity among the parents or ancestors or of ocular disease among parents or relatives.

The older brother, aged 35, had some difficulty in reading while in high school, and in 1943 he consulted a physician because of gradual failure of vision. Vision with glasses was 20/30 in the right eye and 20/200 in the left eye, eccentric. Ophthalmoscopic examination revealed normal disks. Numerous yellowish white spots, situated fairly deep in the retina, were scattered throughout the posterior segments. In the right eye the macular region appeared dull and the foveal reflex was absent. In the left eye the macular region was also dull in appearance and a "hole in the macula" was apparently developing. In the right eye there was a relative central scotoma for blue and red, containing a para-central absolute nucleus. In the left eye there was an absolute central scotoma. Two children, aged 7 and 4 years, were apparently normal in every respect.

The sister, aged 29, noticed that her vision was failing in the fall of 1945. Vision with glasses was 20/30 in the right eye and 20/200 in the left eye. On ophthalmoscopic examination the disks appeared normal. The macula of the right eye appeared swollen, and there was a slight disturbance in pigment and a few small glistening spots in this area. In the left eye the picture was essentially the same, except that the foveal reflex appeared widened. A central scotoma was present in each eye, relative to 1 degree white and absolute to 1 degree blue and red.

The younger brother, aged 31, had recently noted slight disturbance of vision. Objects appeared to quiver in the late afternoon. Vision was 20/20 in the right eye and 20/20 in the left eye. On ophthalmoscopic examination the disks appeared normal, the fovea of each eye dark and the foveal reflex broadened, so that one had the impression that the reflex was situated slightly anterior to the surface of the retina. Surrounding each fovea the retina showed a very narrow, indistinct band of extremely fine stippling. In the right eye there was a small para-central scotoma, and in the left eye there was a narrow ring scotoma. One child, aged 18 months, was apparently healthy.

The cases represented different stages of the same type of macular degeneration. "Hole in the macula," yellowish spots and stippling of the retina have all been described by other authors. The younger brother probably represents the earliest recognizable stage of the disease. In this case the presence of a broadened, anterior foveal reflex and the narrow ring scotoma may be important points in the early diagnosis of the condition. The influence of infection on the development of similar macular lesions has been suggested by several observers. The role of brucellosis in the development of these lesions is extremely doubtful but, is, nevertheless, an interesting coincidence.

#### DISCUSSION

DR. RALPH I. LLOYD: We are indebted to Dr. Burton for this report of a family with hereditary macular degeneration. Few of these lesions ever reach the laboratory, for only eyes presenting a menace to life or to the other eye, or those too painful to bear, ever reach the pathologist. Knowledge of this disease is limited, and only observations on families over a period of years will compensate for the lack of pathologic material. Photographs or paintings should be made from time to time to show the various stages and aspects, of which present information is scant. I hope Dr. Burton will keep this family under

observation for years and will finally give us a report, including the progeny in his survey. If one can awaken the interest of oculists generally, the disease will be better understood and an occasional eye will be obtained, so that eventually the descriptions in textbooks will measure up to the requirements of instruction in our specialty.

DR. ARNOLD KNAPP: May I add that I had the opportunity of seeing recently, after twenty years, one of my patients with macular degeneration to which Dr. Burton referred. This woman has kept the same vision, and the fundus picture has not in any way changed; she has had a number of children, and their eyes are normal.

**Reconstruction of the Upper Lid** (a color film). DR. ALSTON CALLAHAN (by invitation), University, Ala.

The preoperative appearance of a man aged 20 with a deformity of the lid since birth was shown. A large central area of the right upper lid was missing, in the manner of a congenital coloboma.

The surgical procedure, performed with the use of local anesthesia, was shown in detail. Both the medial and the lateral fragments were divided into an anterior lamina of skin and orbicularis muscle, and a posterior lamina of tarsus and conjunctiva. Small rectangular areas were denuded on the margins of the upper lid fragments and on the margin of the lower lid to provide for intermarginal adhesions for the maintenance of tension on each side of the defect: The two parts of the posterior lamina were then joined with mattress sutures (chromic surgical gut 0000).

The anterior fragments could not be joined without further relaxation, for the tension would tear out sutures through them. The medial fragment was too short to furnish needed tissue. The lateral fragment was entirely divided into the laminae, and the anterior lamina of the lid was separated from the lateral palpebral raphe by making an oblique incision upward through the skin at the extremity of the lid. The two parts of the anterior lamina were then joined easily with interrupted sutures (braided silk 0000). The intermarginal adhesions were then made by uniting the small rectangular denuded areas with Wheeler sutures.

To correct the surgical defect caused by the medial displacement of the lateral fragment, the area of skin and muscle lateral to the oblique incision was undermined and advanced medial to the transposed lamina. This incision was then closed with interrupted sutures. Penicillin solution (500 units per cubic centimeter) was applied liberally, and the lids of both sides were bandaged firmly.

After five days all dressings were discontinued, and after seven days the sutures were removed. The lid adhesions were allowed to remain for three months to prevent retraction of the fragments or the formation of a notch. After this time they were divided, and the result as seen two months later was satisfactory functionally and cosmetically.

#### DISCUSSION

DR. WENDELL L. HUGHES: This is a beautiful demonstration of a surgical procedure. I think there is no question about its being a congenital coloboma. In the moving picture, the difference of several

millimeters in the level of the medial canthus on the right and that on the left was very nicely demonstrated. I had the opportunity of operating this afternoon on a baby with a somewhat similar condition in the lower lid, in which the difference in the medial canthus on the affected side was about 5 mm.—an extreme difference. Another child, 4 years old, on whom I operated three weeks ago had a coloboma of the upper lid similar to that illustrated in the moving pictures. There was not so much of a difference in the level of the medial canthus as in the present case. The importance surgically and cosmetically of the two layers in the lid is graphically demonstrated by Dr. Callahan's beautiful presentation.

DR. BYRON SMITH: I should like to ask a question concerning the apparent ptosis. Was that real, or merely due to the light; if it was a real ptosis, what does Dr. Callahan anticipate in the treatment of it?

DR. ALSTON CALLAHAN: The levator palpebrae superioris functions normally, and the apparent ptosis is due to the manner in which the lid was reconstructed. The last photographs shown were made five months after operation. This patient resides in the East and was seen by me only a few days ago, eighteen months after operation. The right lid now more nearly matches the left because of the changes due to the passage of time.

**Ocular Leprosy in Panama** (motion picture). DR. ROBISON D. HARLEY (by invitation), Atlantic City, N. J.

Ocular leprosy is not uncommon in Panama or in the neighboring countries. All patients known to have the disease are confined in the leprosarium of the Canal Zone, where facilities are at hand for careful study.

In a recent study of 150 cases over a period of four years, ocular complications were found in 90 per cent. Fifty-four per cent of the patients had vision of 6/60 or less, and of this number 13 per cent were blind.

Leprosy affects the anterior segment of the eye almost exclusively. The cornea is the most vulnerable of the ocular tissues and was involved in 58 per cent of the cases. The commonest form of keratitis was a typical "chalk dust," superficial, punctate keratitis, which occurred in 34 per cent of all cases. Interstitial keratitis and deep keratitis were common.

Iritis, or evidence of iritis, was found in 50 per cent of the cases. Pinpoint lepromas engrafted on a chronically inflamed iris were frequently seen with the slit lamp.

The limbus was the favorite site of larger lepromas. Lagophthalmos, due to peripheral involvement of the seventh nerve and ectropion were frequently seen.

Absolute corneal anesthesia was rare, but relative loss of corneal sensitivity does occur in severe cases. The conjunctiva appears to be rather resistant to the disease.

Promin® (sodium p, p'-diaminophenylsulfone-N, N'-didextrose sulfonate) was an effective drug in the treatment of leprosy. Secondary infection cleared, and recurrent attacks of iritis were less common.

## DISCUSSION

DR. GEMINIANO DE OCAMPO: I have very little experience with leprosy of the eye. In the Philippines it is true that there are plenty of lepers, but they are segregated in a colony, and we in the department of ophthalmology of the Philippine General Hospital in Manila rarely see a case of leprosy. About ten years ago I examined clinically several patients with lesions of ocular leprosy, but I have not seen them a second time. The disease was of the granulomatous type, affecting the lids and the anterior segment of the eye—the iris, ciliary body, cornea, sclera and episclera.

DR. ARTHUR LINKSZ: What did you do for personal protection?

DR. ROBISON D. HARLEY, Atlantic City, N. J.: First, I was advised to wear gloves and a mask, but the patients resented being treated as untouchables. In order to get the cooperation of these patients for observation and treatment, one must first make friends of them. So I discarded the gloves and mask, and when they saw I was not visibly afraid of them they began to warm up to me. At Palo Seco Leper Colony medical treatment is not compulsory. They attend the dispensary voluntarily. Soon I found the clinic attendance increasing satisfactorily, and I never returned to the gloves and mask.

According to the literature, there have been no cases of doctors or nurses contracting the disease; so I felt relatively safe. The case of Father Damien, on Molokai Island, is one of the few known instances on record in which a normal adult acquired the disease through contact. At the conclusion of the clinic we scrubbed carefully with soap and water and followed with an alcohol wash.

**Malignant Melanoma of the Choroid with Sympathetic Ophthalmia.** DR. HUNTER ROMAINE (by invitation).

A Russian woman aged 50 had a history of a red, painful right eye of one year's standing. Examination revealed a glaucomatous (tension, 90 mm.), severely inflamed eye with corneal edema, a large swollen lens, poor light projection and restricted transillumination. The lens was extracted, followed by return of tension and posterior uveitis, rather typical of sympathetic ophthalmia, in the left eye, with reduction of vision to 20/400.

Permission was gained for enucleation (three months later). General systemic treatment was followed by clearing of the uveitis, revealing optic neuritis, which, in turn, subsided. Normal vision was restored to the remaining eye.

The author discussed the possibility of symptoms of sympathetic ophthalmia developing from the melanoma or after operation and the probable maintenance of vision if the ophthalmia is the true sympathetic type.

## DISCUSSION

DR. BRITAIN F. PAYNE: A section of this eye was presented at a meeting of the Pathology Club in Washington, D. C., last month. It was studied by every one there, including Dr. Verhoeff, who concurred with Dr. Romaine in the diagnosis of sympathetic ophthalmia in the presence of a tumor. Dr. John Reid had just such a case about

fifteen years ago, with a history of the same type. In his closing remarks, Dr. Romaine has consented to show Dr. Reid's slide and to say a few words about the case.

DR. ARNOLD KNAPP: How do you differentiate sympathetic ophthalmia arising from traumatic iridocyclitis after a cataract operation and one secondary to a sarcoma of the choroid? I wish to point out that the sympathetic ophthalmia of the second eye, which shows itself in the form of an optic neuritis, is always a benign form.

DR. LUDWIG VON SALLMANN: Dr. Romaine allowed me to see one of the sections in his case. The changes in the uvea were, in my opinion, consistent with the diagnosis of sympathetic ophthalmia. Since I did not know the surgical history of the case and could not deduce it from the section, I concluded that the sympathetic ophthalmia was connected with the sarcoma.

DR. EMANUEL ROSEN: Dr. Rados, who has studied this problem extensively, has pointed out that in the case of sympathetic ophthalmia following a sarcoma of the choroid, provided serial sections are made, one will usually find a perforation of the globe somewhere; so the element of trauma is introduced, as was done surgically here.

DR. HUNTER H. ROMAINE: Dr. Knapp, I wish I could differentiate the two types of sympathetic ophthalmia. I realize that the etiologic factor, and even the presence of the sympathetic ophthalmia, is controversial in this case; but I thought the case was interesting enough to justify presentation. I wish I were able to make that differentiation.

Dr. John Reid, of Lenox Hill Hospital, has a case in which the eye shows almost the same condition. The patient sustained an injury to the eye and glaucoma developed. A filtration operation was performed, and two weeks later the good eye became inflamed. A diagnosis of sympathetic ophthalmia was made, and on the basis of poor transillumination a tumor was suspected. The exciting eye was removed, and the specimen was shown. The tumor appears somewhat smaller, and it is a little more difficult to make out the uvea. The tumor tissue itself has similarly lined and unlined vessels. The tumor cells are rather difficult to make out, but the same type of infiltration is noted here as in my case; the difference is that endothelioid cells and giant cells could be located in the tissue in his case and not in my case. There is definite lymphocytic infiltration.

# Directory of Ophthalmologic Societies \*

## INTERNATIONAL

### INTERNATIONAL ASSOCIATION FOR PREVENTION OF BLINDNESS

President: Dr. P. Bailliant, 66 Boulevard Saint-Michel, Paris, 6<sup>e</sup>, France.  
Secretary-General: Dr. A. Churchill, 66 Boulevard Saint-Michel, Paris, 6<sup>e</sup>, France.  
All correspondence should be addressed to the Secretariat, 66 Boulevard Saint-Michel, Paris, 6<sup>e</sup>, France.

### INTERNATIONAL COUNCIL OF OPHTHALMOLOGY

President: Prof. F. W. Nordenson, 3 Grefgatan, Stockholm, Sweden.  
Secretary: Dr. Halger Ehlers, Rigshospital, Copenhagen, Denmark.

### INTERNATIONAL ORGANIZATION AGAINST TRACHOMA

President: Dr. A. F. MacCallan, 17 Horseferry Rd., London S. W., England.  
Secretary: Dr. F. Wibaut, P. C. Hoofstraat 145, Amsterdam, Holland.

### PAN-AMERICAN ASSOCIATION OF OPHTHALMOLOGY

President: Dr. Conrad Berens, 301 E. 14th Street, New York 3.  
Secretary: Dr. Thomas D. Allen, 122 So. Michigan Ave., Chicago 2, Ill.  
Place: Interim Meeting: Miami Beach, Fla. Time: March 26-31, 1950; IV  
Pan-American Congress of Ophthalmology early in 1952.

### PAN-AMERICAN ASSOCIATION OF OPHTHALMOLOGY

#### PUERTO RICO CHAPTER

President: Dr. Luis J. Fernandez.  
Secretary: Dr. P. Fernandez.  
Place: San Juan, Puerto Rico.

## FOREIGN

### ALL-INDIA OPHTHALMOLOGICAL SOCIETY

President: Dr. S. A. Rahim, Kachiguda, Hyderabad (Deccan).  
Secretaries: Dr. G. Zachariah, 16 Marshall's Rd., Egmore, Madras. Dr. S. N. Cooper, Laud Mansion, 15 Queen's Rd., Bombay.

### BELGIAN OPHTHALMOLOGIC SOCIETY

President: Dr. L. Weekers, Rue Forgeur 15, Liège.  
Secretary-General: Dr. M. Appelmans, Avenue Ruelens 179, Louvain.  
Place: Bruxelles. Time: January, June and November.

### BOMBAY OPHTHALMOLOGISTS' ASSOCIATION

President: Rotated  
Conveners: Dr. S. N. Cooper and Dr. B. D. Telang, Laud Mansion 21, Queen's Road, Bombay 4.

### BRITISH MEDICAL ASSOCIATION, SECTION ON OPHTHALMOLOGY

President: Mr. O. G. Morgan, 115a Harley St. W. 1, London, England.  
Secretary: Mr. A. G. Cross, 27 Harley St., London W. 1.

### CHENG TU OPHTHALMOLOGICAL SOCIETY

President: Dr. Eugene Chan.  
Secretary: Dr. D. S. Shen, Eye, Ear, Nose and Throat Hospital, Chengtu, Szechuan, China.  
Place: Eye, Ear, Nose and Throat Hospital, Chengtu, Szechuan, China.

\* Secretaries of societies are requested to furnish the information necessary to make this list complete and keep it up to date.

CHINESE OPHTHALMOLOGY SOCIETY

President: Dr. C. H. Chou, 363 Avenue Haig, Shanghai.  
Secretary: Dr. F. S. Tsang, 221 Foochow Rd. Shanghai.

CHINESE OPHTHALMOLOGICAL SOCIETY OF PEIPING

President: Dr. H. T. Pi, Peiping Union Medical College, Peiping.  
Secretary: Dr. C. K. Lin, 180 Hsi-Lo-yen Chienmeng, Peiping.  
Place: Peiping Union Medical College, Peiping. Time: Last Friday of each month.

FOREIGN

DEUTSCHE OPHTHALMOLOGISCHE GESELLSCHAFT HEIDELBERG

President: Professor Dr. med. K. Wessely, München, Universitäts-Augenklinik.  
Secretary: Professor Dr. med. E. Engelking, Heidelberg, Universitäts-Augenklinik.  
Place: Heidelberg. Time: 18.V.1949.

FACULTY OF OPHTHALMOLOGISTS

President: Dr. Frank W. Law, 45 Lincoln's Inn Fields, London, W.C. 2, England.  
Secretary: Dr. J. H. Doggart, F.R.C.S.

GERMAN OPHTHALMOLOGICAL SOCIETY

President: Prof. W. Lohlein, Berlin.  
Secretary: Prof. E. Engelking, Heidelberg.

HUNGARIAN MEDICAL TRADE UNION, SECTION OF OPHTHALMOLOGY

President: I. Csapody, János-Kórház, Budapest, Hungary.  
Secretary: E. Galla, Krisztina Körút 139, Budapest, Hungary.  
Place: Illes u. 15, Budapest, Hungary.

HUNGARIAN OPHTHALMOLOGICAL SOCIETY

President: Prof. G. Horay, Budapest.  
Assistant Secretary: Dr. Stephen de Grósz, University Eye Hospital, No. 1, Illes-ucca 15, Budapest.  
All correspondence should be addressed to the Assistant Secretary.

ISRAEL OPHTHALMOLOGICAL SOCIETY

President: Dr. Aryeh Feigenbaum, 15 Abyssinian Street, Jerusalem.  
Secretary: Dr. E. Sinai, 9 Bialik St., Tel Aviv.

MIDLAND OPHTHALMOLOGICAL SOCIETY

President: Dr. H. Campbell Orr, 8 Summerfield Road, Wolverhampton, England.  
Secretary: Dr. P. Jameson Evans, 51 Calthorpe Rd., Birmingham 3, England.  
Place: Birmingham and Midland Eye Hospital.

NEDERLANDSCH OOGHEELKUNDIG GEZELSCHAP

President: Prof. A. W. Mulock Houwer, Bussum.  
Secretary: Dr. T. A. Vos, Laan v. Meerdervoort 394, the Hague.

NORTH OF ENGLAND OPHTHALMOLOGICAL SOCIETY

President: Mr. J. S. Arkle, 3, Eslington Road, Newcastle-on-Tyne.  
Secretary: Mr. W. M. Muirhead, 70 Upper Hanover Street, Sheffield, 3.  
Place: Manchester Leeds Newcastle, Liverpool, Sheffield & Bradford.  
Time: October to May.

OPHTHALMOLOGICAL AND OTO-LARYNGOLOGICAL SOCIETY OF ALBERTA

President: Dr. R. F. Nicholls, McLeod Bldg., Edmonton.  
Secretary: Dr. Mark R. Levey, Wells Pavillion, University Hospital, Edmonton.

OPHTHALMOLOGICAL SOCIETY OF AUSTRALIA

President: Dr. Arthur H. Joyce, 55 Collins St., Melbourne.  
Secretary: Dr. Arnold L. Lance, 135 Macquarie St., Sydney.  
Place: Melbourne. Time: October 1949.



## OPHTHALMOLOGICAL SOCIETY OF EGYPT

President: Dr. F. Maxwell Lyons, Memorial Ophthalmic Laboratory, Giza.  
 Secretary: Dr. Mahmoud Lutfi, Ophthalmic Hospital, Giza.  
 Place: Dar El Hekmah, 42, Kasr El Ainy, Cairo.

## OPHTHALMOLOGICAL SOCIETY OF HOSPITAL DE NUESTRA SEÑORA DE LA LUZ

Chairman: Dr. Manuel J. Icaza y Dublán, Artes 72, México, D. F., Mexico.  
 Secretary: Dr. Jorge Meyrán, Ezequiel Montes 135, México, D. F., Mexico.  
 Place: Hospital de Nuestras Señora de la Luz. Time: Second Friday of each month.

## OPHTHALMOLOGICAL SOCIETY OF NEW ZEALAND

President: Mr. W. A. Fairclough, Imperial Bldgs., Queen St., Auckland.  
 Secretary: Dr. W. J. Hope-Robertson, Kelvin Chambers, 16 The Terrace, Wellington.

## OPHTHALMOLOGICAL SOCIETY OF SOUTH AFRICA

President: Dr. M. Fine, 82 Lister Bldg., Jeppe St., Johannesburg.  
 Secretary: Dr. R. L. H. Townsend, National Mutual Bldg., Church Sq., Cape Town.

## OPHTHALMOLOGICAL SOCIETY OF THE UNITED KINGDOM

President: F. A. Juler, C.V.O., F.R.C.S.  
 Secretaries: Geoffrey J. O. Bridgeman, M.C., F.R.C.S. Dr. A. C. Cross, F.R.C.S.

## OXFORD OPHTHALMOLOGICAL CONGRESS

Master: Mr. F. A. Williamson-Noble, 27 Harley St., London W. 1, England.  
 Secretary-Treasurer: Dr. Ian C. Fraser, 12 St. John's Hill, Shrewsbury, England.  
 Place: Oxford, England. Time: July.

## PHILIPPINE OPHTHALMOLOGICAL AND OTOLARYNGOLOGICAL SOCIETY

President: Dr. Edmundo Reyes, 288 Gral. Solano, San Miguel, Manila.  
 Secretary-Treasurer: Dr. Carlos V. Yambao, Philippine General Hospital, Manila.

## POLISH OPHTHALMOLOGICAL SOCIETY

President: Prof. Dr. W. Kapuściński, Libelta 14, Poznań.  
 Secretary: Dr. S. Topolski, Piusa 38, Warsaw.  
 Place: Ophthalmic Clinic, Oczki 6, Warsaw. Time: Every two years—Summer.

PUERTO RICO MEDICAL ASSOCIATION, SECTION OF OPHTHALMOLOGY  
AND OTOLARYNGOLOGY

President: Dr. A. Navas Torres, Santurce.  
 Secretary: Dr. A. Laugier, San Juan.  
 Place: Asociacion Medica de Puerto Rico, Santurce. Time: Monthly.

## ROYAL SOCIETY OF MEDICINE, SECTION OF OPHTHALMOLOGY

President: Dr. Montague L. Hine, F.R.C.S.  
 Secretaries: Dr. Arthur Lister. Dr. H. E. Hobbs, 1 Wimpole Street, London, W.1.

## SÃO PAULO SOCIETY OF OPHTHALMOLOGY

President: Dr. Durval Prado, Rua Senador Paulo Egydio, 15-5°-514, São Paulo, Brazil.  
 Secretary: Dr. Rubens Belfort Mattos, Rua B. Stapetininga, 29 F-3° andar, São Paulo, Brazil.

SCOTTISH OPHTHALMOLOGICAL CLUB

President: Dr. Alexander Garrow, 15 Woodside Pl., Glasgow, C. 3.  
Secretary: Dr. John Marshall, 11 Claremont Gardens, Glasgow, C. 3.  
Place: Edinburgh and Glasgow, in rotation. Time: March and October.

SOCIEDAD ARGENTINA DE OFTALMOLOGIA

President: Dr. Diego M. Arguello, Calle 46 No. 655, La Plata.  
Secretary: Dr. Pedro F. Garcia Nocito, Vicente Lopez 1756 A, Buenos Aires.  
Place: Buenos Aires. Time: Third Wednesday of every month.

SOCIEDADE BRASILEIRA DE OFTALMOLOGIA

President: Dr. Natalicio de Farias, R. 13 de maio 23, 17° andar, Rio de Janeiro, Brazil.  
Secretary: Dr. Ismar Pereira, Praca Floriano 55, 5° andar, Rio de Janeiro, Brazil.  
Place: Third Friday every month from April to December.

SOCIEDAD COLOMBIANA DE OFTALMOLOGIA Y DE OTORRINOLARINGOLOGIA

President: Dr. Jorge Suárez-Hoyos, Carrera 5a, no. 13-39, Bogotá, Colombia.  
Secretary: Dr. Fancisco Arango, Calle 20, no. 4-51, Bogotá, Colombia.  
Place: Club Médico. Time: Second Tuesday of every month.  
All correspondence should be addressed to the President.

SOCIEDAD CHILENA DE OFTALMOLOGIA

President: Dr. Italo Martini Zerega, Pedregal, no. 216, Santiago, Chile.  
Secretary: Dr. Adrian Araya Costa, Renaca, no. 34, Santiago, Chile.  
Place: Santiago, Chile.

SOCIEDAD CUBANA DE OFTALMOLOGIA

President: Prof. Lorenzo Comas, Calle D #461, Vedado, Habana, Cuba.  
Secretary: Dr. Oscar F. Horstmann, Calle 5ta. #702, Vedado, Habana, Cuba.  
Time: Second Tuesday of every month.

SOCIEDAD MEXICANA DE OFTALMOLOGIA

President: Dr. Feliciano Palomino Dena, Londres 44, México, D. F.  
Secretary: Dr. Teodulo Agundis Jr., Lucerna 63, México, D. F.  
Place: Escuela Nacional de Medicina, Venezuela 4, México, D. F. Time: 8:30 p. m., first Tuesday of each month.

SOCIEDAD OFTALMOLOGIA DEL LITORAL, ROSARIO (ARGENTINA)

President: Dr. Juan Manuel Vila Ortiz, Italia 663, Rosario.  
Secretary: Dr. Maximo Carlos Soto, Rosario.  
Place: Rosario. Time: Last Saturday of every month, April to November. All correspondence should be addressed to the President.

SOCIEDAD DE OFTALMOLOGIA DE CÓRDOBA

Chairman: Dr. Roberto Obregón Oliva.  
Secretary: Dr. Alberto Urrets Zavalía (hijo), 27 de Abril 255, Córdoba, Argentina.

SOCIEDAD DE OFTALMOLOGIA DE GUADALAJARA

President: Dr. Enrique Avalos Gonzales, Morelos 479, Guadalajara, Mexico.  
Secretary: Dr. Jesus Gomez Plasencia, Pedro Moreno 587, Guadalajara, Mexico.  
Place: Edificio Lutecia, Desp. 101. Time: Second Thursday of each month.

SOCIEDAD DE OFTALMOLOGIA DEL LITORAL

President: Dr. Juan Manuel Vila Ortiz, Córdoba 1915, Rosario, Argentina.  
Secretary: Dr. Carlos M. Soto.  
Place: Rosario, Argentina. Time: Last Sunday in every month.

## SOCIEDADE DE OFTALMOLOGIA DEL NORTE

President: Dr. Jorge Luis Castillo, Mendoza 421, Tucumán, Argentina.  
 Secretary: Dr. Felix Berman, San Lorenzo 345, Tucumán, Argentina.  
 Place: Mendoza 421, Tucumán, Argentina.

## SOCIEDADE DE OFTALMOLOGIA DE MINAS GERAIS

President: Prof. Hilton Rocha.  
 Secretary: Dr. Oswaldo Carvalho.  
 Place: Belo Horizonte, Minas Gerais, Brazil.

SOCIEDADE DE OFTALMOLOGIA E OTORINOLARINGOLOGIA DO  
RIO GRANDE DO SUL

President: Dr. Luiz Assumpção Osorio, Edificio Vera Cruz, Apartamento 134.  
 Porto Alegre, Rio Grande do Sul.  
 Secretary: Dr. Fernando Voges Alves, Caixa Postal 928, Porto Alegre, Rio Grande  
 do Sul.

## SOCIEDADE DE OFTALMOLOGIA E OTO-RHINO-LARYNGOLOGIA DO BAHIA

President: Dr. Theonilo Amorim, Barra Avenida, Bahia, Brazil.  
 Secretary: Dr. Adroaldo de Alencar, Brazil.  
 All correspondence should be addressed to the President.

## SOCIETA OFTALMOLOGICA ITALIANA

President: Prof. Giuseppe Ovio, Via Ombrone, 14 Roma.  
 Secretary: Prof. E. Leonardi, Piazza degli Eroi, 11 Roma.  
 Place: Roma Piazza degli Eroi 11.

## SOCIÉTÉ FRANÇAISE D'OPHTALMOLOGIE

Secretary: Dr. Edward Hartmann, Hospital Lariboisière, Paris 10.

## SOCIETY OF SWEDISH OPHTHALMOLOGISTS

President: Prof. S. Larsson, Lund, Sweden.  
 Secretary: Dr. K. O. Granström, Södermalmstorg 4, Stockholm.

## SOUTHERN OPHTHALMOLOGICAL SOCIETY, ENGLAND

President: Dr. C. C. Schurr, 29 The Drive, Hove, Sussex.  
 Secretary: Mr. Nigel Cridland, 25 Craneswater Pk., Southsea, England.  
 Time: From March to October.

## NATIONAL

AMERICAN MEDICAL ASSOCIATION, SCIENTIFIC ASSEMBLY, SECTION  
ON OPHTHALMOLOGY

Chairman: Dr. A. Ray Irvine, Beverly Hills, Calif.  
 Secretary: Dr. Trygve Gundersen, 101 Bay State Rd., Boston.  
 Place: San Francisco. Time: June 26-30, 1950.

AMERICAN ACADEMY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY,  
SECTION ON OPHTHALMOLOGY

President: Dr. C. H. McCaskey, 20 N. Meridian St., Indianapolis, Ind.  
 Executive Secretary-Treasurer: Dr. William L. Benedict, 100-1st. Ave. Bldg.,  
 Rochester, Minn.

## AMERICAN OPHTHALMOLOGICAL SOCIETY

President: Dr. Bernard Samuels, 57 W. 57th St., New York.  
 Secretary-Treasurer: Dr. Maynard C. Wheeler, 30 W. 59th St., New York 19.

ASSOCIATION FOR RESEARCH IN OPHTHALMOLOGY, INC.

Chairman: Dr. Robert J. Masters, 23 E. Ohio St., Indianapolis.

Secretary-Treasurer: Dr. James H. Allen, University Hospitals, Iowa City.

CANADIAN MEDICAL ASSOCIATION, SECTION ON OPHTHALMOLOGY

President: Dr. R. G. C. Kelly, 14 Lynwood Ave., Toronto.

Secretary: Dr. J. Clement McCulloch, 380 Medical Arts Bldg., Toronto.

CANADIAN OPHTHALMOLOGICAL SOCIETY

President: Dr. Jules Brault, 418 Sherbrooke St. East, Montreal, Quebec.

Secretary-Treasurer: Dr. J. F. A. Johnston, 174 St. George St., Toronto 5.

NATIONAL SOCIETY FOR THE PREVENTION OF BLINDNESS, INC.

President: Mr. Mason H. Bigelow, 1790 Broadway, New York 19.

Secretary: Dr. Franklin M. Foote, 1790 Broadway, New York 19.

SECTIONAL

ACADEMY OF MEDICINE OF NORTHERN NEW JERSEY, SECTION ON  
EYE, EAR, NOSE AND THROAT

President: Dr. Anthony M. Sellitto, 115 Connett Pl., South Orange.

Secretary: Dr. W. F. Grant, 1224 Salem Avenue, Hillside, N. J.

Place: 91 Lincoln Park South, Newark. Time: 8:45 p. m., second Monday of each month, October to May.

ARK-LA-TEX OTO-OPHTHALMIC SOCIETY

President: Dr. W. Griffin Jones, 4421 Creswell, Shreveport, La.

Secretary: Dr. F. L. Bryant, Shreveport, La.

Place: Shreveport Club. Time: 6:30 p.m. first Monday, Sept. to June (incl.).

CENTRAL ILLINOIS SOCIETY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

President: Dr. Clifton S. Turner, 216 Parkside Dr., Peoria.

Secretary-Treasurer: Dr. Philip R. McGrath, Jefferson Bldg., Peoria.

Place: Various Central Illinois towns. Time: Two meetings a year.

CENTRAL WISCONSIN SOCIETY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

President: Dr. Edward J. Zeiss, 103 W. College Ave., Appleton, Wis.

Secretary: Dr. G. L. McCormick, 650 S. Central Ave., Marshfield.

HAWAII EYE, EAR, NOSE AND THROAT SOCIETY

President: Dr. Robert T. Wong, 1147 Union Street, Honolulu.

Secretary-Treasurer: Dr. Ogden Pinkerton, Young Hotel Bldg., Honolulu.

Place: Pacific Club, Honolulu. Time: Third Thursday of each month.

INTER-MOUNTAIN OTO-OPHTHALMOLOGICAL SOCIETY

President: Dr. Ralph O. Porter, 50 North 1st East, Logan.

Secretary-Treasurer: Dr. Harry O. Frazier, 707 Medical Arts Bldg., Salt Lake.

Place: University Club, Salt Lake City. Time: 7:00 p. m., third Monday of each month, September through May.

NEW ENGLAND OPHTHALMOLOGICAL SOCIETY

President: Dr. Benjamin Sachs, 520 Beacon Street, Boston.

Secretary-Treasurer: Dr. Garrett L. Sullivan, 101 Bay State Rd., Boston 15.

Place: Massachusetts Eye and Ear Infirmary, 243 Charles St., Boston. Time: 8 p. m., third Wednesday of each month from November to April, inclusive.

PACIFIC COAST OTO-OPHTHALMOLOGICAL SOCIETY

President: Dr. Guy Boyden, 1735 N. Wheeler Ave., Portland 12, Ore.

Secretary-Treasurer: Dr. C. Allen Dickey, 450 Sutter St., San Francisco 8.

Place: San Francisco. Time: Spring, 1950.

### PUGET SOUND ACADEMY OF OPHTHALMOLOGY AND OTO-LARYNGOLOGY

President: Dr. Robert Wightman, 1114 Boylston Ave., Seattle, Wash.  
 Secretary-Treasurer: Dr. Barton E. Peden, 301 Stimson Bldg., Seattle 1, Wash.  
 Place: Seattle or Tacoma, Wash. Time: Third Tuesday of each month except June, July and August.

### ROCK RIVER VALLEY EYE, EAR, NOSE AND THROAT SOCIETY

President: Dr. Robert C. Fringer, Rockford News Tower, Rockford, Ill.  
 Secretary-Treasurer: Dr. Vernon C. Voltz, 806 Gas-Electric Bldg., Rockford, Ill.  
 Place: Rockford, Ill., or Janesville or Beloit, Wis. Time: Third Tuesday of each month from October to April, inclusive.

### SAGINAW VALLEY ACADEMY OF OPHTHALMOLOGY & OTOLARYNGOLOGY

President: Dr. V. E. Cortopassi, 324 S. Washington Avenue, Saginaw, Mich.  
 Secretary: Dr. A. J. Cortopassi, 324 S. Washington Ave., Saginaw, Mich.  
 Place: Saginaw, Bay City or Flint, Mich. Time: Second Tuesday evening.

### SIoux VALLEY EYE AND EAR ACADEMY

President: Dr. M. W. Eggers, Sioux Falls, S. D.  
 Secretary-Treasurer: Dr. W. P. Davey, 2101 Grandview Blvd., Sioux City 18, Iowa.

### SOUTHERN MEDICAL ASSOCIATION, SECTION ON OPHTHALMOLOGY AND OTOLARYNGOLOGY

President: Dr. Murdock Euen, Atlanta, Georgia.  
 Secretary: Dr. Edley H. Jones, 1301 Washington Street, Vicksburg, Miss.  
 Place: Cincinnati, Ohio. Time: November 15-17.

### SOUTHWESTERN ACADEMY OF EYE, EAR, NOSE AND THROAT

President: Dr. H. L. Brehmer, 221 W. Central Ave., Albuquerque, N. Mex.  
 Secretary: Dr. A. E. Cruthirds, 1011 Professional Bldg., Phoenix, Ariz.

### SOUTHWESTERN MICHIGAN TRIOLOGICAL SOCIETY

President: Dr. W. M. Dodge, 716 First National Bank Bldg., Battle Creek.  
 Secretary-Treasurer: D. Kenneth Lowe, 25 W. Michigan Ave., Battle Creek.  
 Time: Last Thursday of September, October, November, March, April and May.

### WESTERN PENNSYLVANIA EYE, EAR, NOSE AND THROAT SOCIETY

President: Dr. Harold M. Griffith, Johnstown, Pa.  
 Secretary-Treasurer: Dr. Fred E. Murdock, 28½ W. Scribner St., Dubois.

## STATE

### ARKANSAS STATE MEDICAL SOCIETY, EYE, EAR, NOSE AND THROAT SECTION

President: Dr. C. G. Hinkle, Batesville, Arkansas.  
 Secretary: Dr. K. W. Cosgrove, 115 E. Capitol, Little Rock.  
 Place: Little Rock, Arkansas. Time: Second week in April.

### COLORADO OPHTHALMOLOGICAL SOCIETY

President: Dr. Leonard Swigert, Republic Bldg., Denver 2.  
 Secretary: Dr. James C. Strong Jr., 209 16th Street, Denver 2.  
 Place: University of Colorado Medical Center, Denver. Time: 3:00 p. m., third Saturday of each month, September to May, inclusive.

### CONNECTICUT STATE MEDICAL SOCIETY, SECTION ON EYE, EAR, NOSE AND THROAT

President: Dr. P. W. Snelling, 85 Jefferson Street, Hartford, Conn.  
 Secretary-Treasurer: Dr. Max Alpert, 881 Lafayette St., Bridgeport, Conn.

GEORGIA SOCIETY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

President: Dr. Lester A. Brown, 137 Doctors Bldg., Atlanta, Georgia  
 Secretary-Treasurer: Dr. B. E. Collins, 701 Elizabeth St., Waycross.  
 Place: Oglethorpe Hotel. Time: March 1950.

INDIANA ACADEMY OF OPHTHALMOLOGY AND OTO-LARYNGOLOGY

President: Dr. Byron Lingemann, Crawfordsville, Ind.  
 Secretary: Dr. Myron S. Harding, 23 E. Ohio St., Indianapolis.

IOWA ACADEMY OF OPHTHALMOLOGY AND OTO-LARYNGOLOGY

President: Dr. Dean M. Lierle, University Hospital, Iowa City, Iowa.  
 Secretary-Treasurer: Dr. C. A. Noe, 102-3rd Ave. S.E., Cedar Rapids, Iowa.

KANSAS STATE MEDICAL SOCIETY, SECTION ON OPHTHALMOLOGY  
 AND OTOLARYNGOLOGY

President: Dr. Clifford Mullen, 1409 Minnesota Ave., Kansas City, Kans.  
 Secretary: Dr. Morris J. Ryan, 905 N. 7th St., Kansas City.

LOUISIANA-MISSISSIPPI OPHTHALMOLOGICAL AND OTOLARYNGOLOGICAL SOCIETY

President: Dr. William Wagner, 921 Canal Street, New Orleans, La.  
 Secretary: Dr. Edley H. Jones, 1301 Washington St., Vicksburg, Miss.

MEDICAL SOCIETY OF THE STATE OF PENNSYLVANIA, SECTION ON  
 EYE, EAR, NOSE AND THROAT DISEASES

Chairman: Dr. William T. Hunt Jr., 1205 Spruce St., Philadelphia 7.  
 Secretary: Dr. Gabriel Tucker, 250 S. 18th St., Philadelphia 3.

MICHIGAN STATE MEDICAL SOCIETY, SECTION OF OPHTHALMOLOGY  
 AND OTOLARYNGOLOGY

Chairman: Dr. Ralph H. Gilbert, 110 Fulton St. E., Grand Rapids.  
 Secretary: Dr. Walter Z. Rundles, 620 Maxine Ave., Grand Rapids.

MINNESOTA ACADEMY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

President: Dr. Avery Prangen, Mayo Clinic, Rochester.  
 Secretary-Treasurer: Dr. Frank Adair, 822 Lawry Medical Arts Bldg., St. Paul 2,  
 Minn.  
 Place: Minneapolis Club. Time: 6:00 p. m., second Friday of each month from  
 October to May.

MONTANA ACADEMY OF OTO-OPHTHALMOLOGY

President: Dr. J. H. Herring, Lewistown.  
 Secretary: Dr. Fritz D. Hurd, 309 Medical Arts Bldg., Great Falls.

NEBRASKA ACADEMY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

President: Dr. W. Howard Morrison, 1500 Medical Arts Bldg., Omaha.  
 Secretary-Treasurer: Dr. John Peterson, 1307 N St., Lincoln.

NEW JERSEY STATE MEDICAL SOCIETY, SECTION ON OPHTHALMOLOGY,  
 OTOLOGY AND RHINOLARYNGOLOGY

Chairman: Dr. A. M. K. Maldeis, 117 N. 6th St., Camden.  
 Secretary: Dr. Albert F. Moriconi, 438 Hamilton Ave., Trenton, N. J.  
 Place: Atlantic City. Time: May 1950.

NEW YORK STATE MEDICAL SOCIETY, EYE, EAR, NOSE AND  
 THROAT SECTION

Chairman: Dr. Thomas H. Johnson, 30 W. 59th St., New York.  
 Secretary: Dr. Darrell G. Voorhees, 135 E. 65th St., New York 21.

## NORTH CAROLINA EYE, EAR, NOSE AND THROAT SOCIETY

President: Dr. J. A. Harrill, Bowman Gray School of Medicine, Winston-Salem.  
 Secretary: Dr. MacLean B. Leath,

## NORTH DAKOTA ACADEMY OF OPHTHALMOLOGY AND OTO-LARYNGOLOGY

President: Dr. George C. Foster, Fargo.  
 Secretary-Treasurer: Dr. M. T. Lampert, Minot.

## OREGON ACADEMY OF OPHTHALMOLOGY AND OTO-LARYNGOLOGY

President: Dr. C. W. Kuhn, 1020 S. W. Taylor St., Portland 5.  
 Secretary: Dr. Richard Fixott, 1020 S. W. Taylor St., Portland 5.  
 Place: Heathman Hotel, Portland. Time: 6:30 p. m., third Tuesday of each month.

## PENNSYLVANIA ACADEMY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

President: Dr. D. S. DeSito, 1006 Highland Bldg., Pittsburgh, Pa.  
 Secretary: Dr. Benjamin F. Souders, 143 N. 6th St., Reading.

## RHODE ISLAND OPHTHALMOLOGICAL AND OTOLOGICAL SOCIETY

Acting President: Dr. N. Darrell Harvey, 112 Waterman St., Providence.  
 Secretary-Treasurer: Dr. Linley C. Happ, 124 Waterman St., Providence.  
 Place: Rhode Island Medical Society, Library, Providence. Time: 8:30 p. m., second Thursday in October, December, February and April.

## SOUTH CAROLINA SOCIETY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

President: Dr. Pierre C. Jenkins, 155 Wentworth, Charleston.  
 Secretary-Treasurer: Dr. Roderick Macdonald, 330 E. Main St., Rock Hill.  
 Place: Greenville, South Carolina. Time: Sept. 12-15.

## TENNESSEE ACADEMY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

President: Dr. George Burchfield, Maryville.  
 Secretary-Treasurer: Dr. Sam H. Sanders, 1089 Madison Ave., Memphis.

## TEXAS OPHTHALMOLOGICAL AND OTO-LARYNGOLOGICAL SOCIETY

President: Dr. August J. Streit, 811 Fisk Bldg., Amarillo, Texas.  
 Secretary: Dr. John L. Matthews, 414 Navarro Street, San Antonio.  
 Place: Gunter Hotel, San Antonio. Time: Dec. 23, 1949.

## VIRGINIA SOCIETY OF OTO-LARYNGOLOGY AND OPHTHALMOLOGY

President: Dr. Francis H. McGovern, 105 S. Union St., Danville.  
 Secretary: Dr. Peter Pastore, Richmond, Va.

## WEST VIRGINIA ACADEMY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

President: Dr. Garnett P. Morison, Charles Town, W. Va.  
 Secretary: Dr. Melvin W. McGehee, Huntington, W. Va.

## LOCAL

## AKRON ACADEMY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

President: Dr. V. C. Malloy, Second National Bldg., Akron 8, Ohio.  
 Secretary-Treasurer: Dr. A. L. Peter, 406 Akron Savings & Loan Bldg., Akron 8, Ohio.  
 Place: Akron City Club. Time: 6:30 p. m., first Monday in January, March, May and November.

## ATLANTA EYE, EAR, NOSE AND THROAT SOCIETY

President: Dr. Russell Burke, 490 Peachtree St., N. E., Atlanta, Ga.  
 Secretary: Dr. James T. King, 384 Peachtree St., Atlanta, Ga.  
 Place: Academy of Medicine. Time: 7:30 p. m., fourth Monday of each month from October to May.

BALTIMORE MEDICAL SOCIETY, SECTION ON OPHTHALMOLOGY

President: Dr. James I. Moore, 11 E. Chase St., Baltimore 2.  
 Secretary: Dr. Elliott Randolph, 11 E. Chase St., Baltimore 2.  
 Place: Medical and Chirurgical Faculty, 1211 Cathedral St. Time: 8:30 p. m.,  
 fourth Thursday of each month from October to March.

BIRMINGHAM EYE, EAR, NOSE AND THROAT CLUB

President: Each member, in alphabetical order.  
 Secretary: Dr. David A. McCoy, Woodward Bldg., Birmingham, Ala.  
 Place: Thomas Jefferson Hotel. Time: 8:30 p. m., second Tuesday of each month,  
 September to May, inclusive.

BROOKLYN OPHTHALMOLOGICAL SOCIETY

President: Dr. Frank E. Mallon, 1 Hanson Pl., Brooklyn 16.  
 Secretary-Treasurer: Dr. Louis Freimark, 256 Rochester Ave., Brooklyn 13.  
 Place: Brooklyn Eye and Ear Hospital, Greene Ave. and Cumberland St. Time:  
 8:15 p. m., third Thursday in February, April, October and December.

BUFFALO OPHTHALMOLOGIC CLUB

President: Dr. Arthur L. Bennett, 147 Linwood Ave., Buffalo.  
 Secretary-Treasurer: Dr. Herbert R. Reitz, 446 Linwood Ave., Buffalo 9.  
 Place: Park Lane. Time: Second Thursday of each month from October  
 to May.

CENTRAL NEW YORK EYE, EAR, NOSE AND THROAT SOCIETY

President: Dr. Everett Wood, Auburn, N. Y.  
 Secretary-Treasurer: Dr. Alfred W. Doust, 306 State Tower Bldg., Syracuse.  
 Place: Syracuse. Time: Quarterly.

CHATTANOOGA SOCIETY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

President: Each member, in alphabetical order.  
 Secretary: Dr. Willard H. Steele Jr., 552 McCallie Ave., Chattanooga, Tenn.  
 Place: Mountain City Club. Time: Third Thursday of each month from  
 September to May.

CHICAGO OPHTHALMOLOGICAL SOCIETY

President: Dr. Derrick Vail, 700 N. Michigan Ave., Chicago.  
 Secretary: Dr. J. R. Fitzgerald, 3215 W. North Avenue, Chicago.  
 Place: Illini Union Bldg. Time: 7:30 p. m., third Monday of each month from  
 October to May.

CINCINNATI OPHTHALMOLOGIC CLUB

Chairman: Rotate alphabetically.  
 Secretary: Dr. Josef D. Weintraub, Provident Bank Bldg., Cincinnati 2, Ohio.  
 Place: As announced. Time: 8:00 p. m., second Friday of each month from  
 November to May, inclusive.

CLEVELAND OPHTHALMOLOGICAL CLUB

President: Dr. G. L. Miller, 14805 Detroit Avenue, Lakewood, Ohio.  
 Secretary: Dr. W. P. Chamberlain, 7405 Detroit Avenue, Cleveland, Ohio.  
 Place: Hotel Statler, Cleveland. Time: Second Tuesday in November, January,  
 February and April.

COLLEGE OF PHYSICIANS, PHILADELPHIA, SECTION ON OPHTHALMOLOGY

President: Dr. Perce de Long, 37 S. 20th St., Philadelphia.  
 Clerk: Dr. M. Luther Kauffman, Medical Arts Bldg., Jenkintown, Pa.  
 Place: College of Physicians Bldg. Time: 8:15 p. m., third Thursday of every  
 month from October to May, inclusive.



## COLUMBUS EYE, EAR, NOSE AND THROAT SOCIETY

President: Dr. Claud Perry, 40 South 3rd Street, Columbus, Ohio.  
 Secretary-Treasurer: Dr. Vernon D. Stephens, 9 Butler Avenue, Columbus, Ohio.  
 Place: University Club. Time: 6:00 p. m., first Monday of each month, from October to May, inclusive.

## CORPUS CHRISTI EYE, EAR, NOSE AND THROAT SOCIETY

President: Dr. B. B. Friedman, Jones Bldg., Corpus Christi, Texas.  
 Secretary: Dr. S. K. Stroud, Medical Professional Bldg., Corpus Christi, Texas.  
 Place: Nueces Hotel. Time: 6:30 p. m., third Tuesday of each month from October to May.

## DALLAS ACADEMY OF OPHTHALMOLOGY AND OTO-LARYNGOLOGY

President: Dr. C. A. Hoefler, 1719 Pacific Ave., Dallas, Texas.  
 Secretary: Dr. W. B. Wilkinson, Tenth and Zangs, Dallas, Texas.  
 Place: Melrose Hotel. Time: 6:30 p. m., first Tuesday of each month from October to June. The November, January and March meetings are devoted to clinical work.

## DES MOINES ACADEMY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

President: Dr. Byron Merkel, 1112 Equitable Bldg., Des Moines, Iowa.  
 Secretary-Treasurer: Dr. H. H. Gurau, 213 Bankers Trust Bldg., Des Moines, Iowa.  
 Place: Des Moines Club. Time: Second Monday of every month from September to May.

## DETROIT OPHTHALMOLOGICAL CLUB

Chairman: Members rotate alphabetically.  
 Secretary: Dr. Wesley G. Reid, 974 Fisher Bldg., Detroit 2.  
 Place: Wayne County Medical Society. Time: Second Monday of each month, November to April, inclusive.

## DETROIT OPHTHALMOLOGICAL SOCIETY

President: Dr. Aaron Ricker, Pontiac, Mich.  
 Secretary: Dr. A. P. Wilkinson, 974 Fisher Bldg., Detroit 2.  
 Place: L'Aiglon-Fisher Bldg. Time: 6:30 p. m., third Thursday of each month from November to April, inclusive.

## EASTERN NEW YORK EYE, EAR, NOSE AND THROAT ASSOCIATION

President: Dr. John H. Sulzman, 1831 Fifth Ave., Troy, N. Y.  
 Secretary-Treasurer: Dr. E. Martin Freund, 762 Madison Ave., Albany 3.  
 Place: Albany, Troy, Schenectady, rotating monthly. Time: 8 p. m., first Thursday of each month, from October to June.

## FORT WORTH EYE, EAR, NOSE AND THROAT SOCIETY

President: Dr. John Eschenbrenner, 306 W. Broadway, Fort Worth, Texas.  
 Secretary-Treasurer: Dr. C. Keith Barnes, 921 Neil P. Anderson Bldg., Fort Worth 2, Texas.  
 Place: All Saints Hospital. Time: 6:30 p. m., first Friday of each month except July and August.

HOUSTON ACADEMY OF MEDICINE, OPHTHALMOLOGICAL AND  
OTO-LARYNGOLOGICAL SECTION

President: Dr. Norma B. Elles, Niels Esperson Bldg., Houston, Texas.  
 Secretary: Dr. R. Marion Johnson, Medical Arts Bldg., Houston, Texas.  
 Place: River Oaks Country Club. Time: 6:30 p. m., second Thursday of each month from October to June.

INDIANAPOLIS OPHTHALMOLOGICAL AND OTOLARYNGOLOGICAL SOCIETY

President: Dr. Kenneth L. Craft, 1002 Hume Mansur Bldg., Indianapolis 4.  
 Secretary: Dr. J. Lawrence Sims, 809 Hume Mansur Bldg., Indianapolis 4.  
 Place: Indianapolis Athletic Club. Time: 6:30 p. m., second Thursday of each month from November to May.

KANSAS CITY SOCIETY OF OPHTHALMOLOGY AND OTO-LARYNGOLOGY

President: Dr. John McLeod, Argyle Bldg., Kansas City, Mo.  
 Secretary: Dr. James W. May, 906 Grand Ave., Kansas City, Mo.  
 Time: 6:00 p. m., third Thursday of each month from November to May. The November, January and March meetings are devoted to clinical work.

LONG BEACH EYE, EAR, NOSE AND THROAT SOCIETY

President: Dr. Orville W. Cole, 125 E. 8th St., Long Beach 2, Calif.  
 Secretary: Dr. Edmund Godwin, 117 E. 8th St., Long Beach, Calif.  
 Place: Seaside Memorial Hospital. Time: 6:15 p. m., third Wednesday of each month from October to May.

LOS ANGELES OPHTHALMOLOGICAL SOCIETY

President: Dr. William Endres, 523 W. 6th St., Los Angeles, Calif.  
 Secretary: Dr. Robert A. Norene, 727 W. 7th St., Los Angeles 14.  
 Place: 3550 Wilshire Blvd., Los Angeles. Time: 6:30 p. m., third Tuesday of each month, September through June.

LOS ANGELES SOCIETY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

President: Dr. Warren A. Wilson, 1930 Wilshire Blvd., Los Angeles 5.  
 Secretary-Treasurer: Dr. Victor Goodhill, 2007 Wilshire Blvd., Los Angeles 5.  
 Place: Los Angeles County Medical Association Bldg., 1925 Wilshire Blvd.  
 Time: 6:00 p. m., fourth Monday of each month from September to May, inclusive.

LOUISVILLE EYE AND EAR SOCIETY

President: Dr. Joseph S. Heitger, Heyburn Bldg., Louisville, Ky.  
 Secretary-Treasurer: Dr. J. W. Fish, 321 W. Broadway, Louisville, Ky.  
 Place: Brown Hotel. Time: 6:30 p. m., second Thursday of each month from September to May, inclusive.

LOWER ANTHRACITE EYE, EAR, NOSE AND THROAT SOCIETY

Chairman: Each member in alphabetical order.  
 Secretary: Dr. James J. Monohan, 31 S. Jardin St., Shenandoah, Pa.

MEDICAL SOCIETY OF THE DISTRICT OF COLUMBIA, SECTION OF  
 OPHTHALMOLOGY AND OTOLARYNGOLOGY

Chairman: Dr. P. S. Constantinople, 1835 I St. N. W., Washington.  
 Secretary: Dr. Frazier Williams, 1801 I St. N. W., Washington.  
 Place: 1718 M St. N. W. Time: 8 p. m., third Friday of each month from October to April, inclusive.

MEMPHIS SOCIETY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

Chairman: Each member, in alphabetical order.  
 Secretary: Dr. Sam H. Sanders, 1089 Madison Ave., Memphis, Tenn.  
 Place: Eye Clinic of Memphis Eye, Ear, Nose and Throat Hospital. Time: 8 p. m., second Tuesday of each month from September to May.

MILWAUKEE OTO-OPHTHALMIC SOCIETY

President: Dr. S. S. Blankstein, 208 E. Wisconsin Avenue, Milwaukee 2.  
 Secretary-Treasurer: Dr. J. P. Wild, 161 W. Wisconsin Avenue, Milwaukee.  
 Place: Athletic Club. Time: 6:30 p. m., fourth Tuesday of each month from October to May.

## MONTGOMERY COUNTY MEDICAL SOCIETY

Chairman: Dr. H. V. Dutrow, 1040 Fidelity Medical Bldg., Dayton, Ohio.  
 Secretary-Treasurer: Dr. Maitland D. Place, 981 Reibold Bldg., Dayton, Ohio.  
 Place: Van Cleve Hotel. Time: 6:30 p. m., first Tuesday of each month from October to June, inclusive.

## MONTREAL OPHTHALMOLOGICAL SOCIETY

President: Dr. B. Alexander, Medical Arts Bldg., Montreal 25, Canada.  
 Secretary: Dr. R. Cloutier, Medical Arts Bldg., Montreal 25, Canada.  
 Time: Second Thursday of October, December, February and April.

## NASHVILLE ACADEMY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

President: Dr. James B. Miller, S. Garden Street, Columbia, Tenn.  
 Secretary: Dr. N. B. Morris, 647 Doctors Bldg., Nashville 3, Tenn.  
 Place: James Robertson Hotel. Time: 6:30 p. m., third Monday of each month from October to May.

## NEW ORLEANS OPHTHALMOLOGICAL AND OTOLARYNGOLOGICAL SOCIETY

President and Secretary: Dr. Mercer G. Lynch, Ochsner Clinic, New Orleans 15, La.  
 Place: Charity Hospital. Time: 8 p. m., first Tuesday of every month.

## NEW YORK ACADEMY OF MEDICINE, SECTION OF OPHTHALMOLOGY

Chairman: Dr. Wendell L. Hughes, 131 Fulton Ave., Hempstead, N. Y.  
 Secretary: Dr. Isadore Givner, 108 E. 66th St., New York 21.  
 Place: Academy of Medicine. Time: 8:30 p. m., third Monday of every month from October to May, inclusive.

## NEW YORK SOCIETY FOR CLINICAL OPHTHALMOLOGY

President: Dr. Sidney A. Fox, 63 E. 75th Street, New York.  
 Secretary: Dr. Leon Ehrlich, 211 Central Park W., New York.  
 Place: New York Academy of Medicine, 2 E. 103d St. Time: 8 p. m., first Monday of each month from October to May, inclusive.

## OKLAHOMA CITY ACADEMY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

President: Dr. Charles A. Royer, 1221 N. W. 19th St., Oklahoma City.  
 Secretary: Dr. C. W. McClure, 1005 Medical Arts Bldg., Oklahoma City.  
 Place: University Hospital. Time: 7:30 p. m., first Tuesday of each month from September to June.

## OMAHA AND COUNCIL BLUFFS OPHTHALMOLOGICAL AND OTOLARYNGOLOGICAL SOCIETY

President: Dr. T. T. Smith, 211 Medical Arts Bldg., Omaha.  
 Secretary-Treasurer: Dr. George T. Alliband, 1020 Medical Arts Bldg., Omaha 2.  
 Place: Omaha Club, 20th and Douglas Sts., Omaha. Time: 6 p. m. dinner; 7 p. m. program; third Wednesday of each month from October through April.

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President: Dr. Thomas Sanfacon, 340 Park Ave., Paterson, N. J.  
 Secretary-Treasurer: Dr. J. Averbach, 435 Clifton Ave., Clifton, N. J.  
 Place: Doctors Lounge, Paulsen Medical and Dental Bldg. Time: 8 p. m., last Tuesday of each month except June, July and August.

## PHILADELPHIA COUNTY MEDICAL SOCIETY, EYE SECTION

President: Dr. Alfred Cowan, 1930 Chestnut Street, Philadelphia 3, Pa.  
 Secretary: Dr. L. Waller Deichler, 1930 Chestnut St., Philadelphia 3.  
 Time: First Thursday of each month from October to May.

PITTSBURGH OPHTHALMOLOGICAL SOCIETY

President: Dr. John S. Plumer, 121 University Place, Pittsburgh.  
 Secretary: Dr. Samuel D. Evans, 1501-1502 Park Bldg., Pittsburgh 22.  
 Place: Pittsburgh Academy of Medicine Bldg. Time: 8:00 p. m., fourth Monday of each month, except June, July, August and September.

READING EYE, EAR, NOSE AND THROAT SOCIETY

President: Dr. W. J. Hertz, 125 N. 8th Street, Allentown, Pa.  
 Secretary: Dr. Paul C. Craig, 232 N. 5th St., Reading, Pa.  
 Place: Wyomissing Club. Time: 6:00 p. m., third Wednesday of each month from September to July.

RICHMOND EYE, EAR, NOSE AND THROAT SOCIETY

President: Dr. Clifford A. Folkes, Professional Bldg., Richmond, Va.  
 Secretary: Dr. W. F. Bryce, 4920 New Kent Road, Richmond, Va.  
 Place: Commonwealth Club. Time: 6 p. m., fifth Tuesday of January, March, May and October.

ROCHESTER EYE, EAR, NOSE AND THROAT CLUB

President: Dr. Frank Barber, 75 S. Fitzhugh St., Rochester, N. Y.  
 Secretary-Treasurer: Dr. Charles T. Sullivan, 277 Alexander St., Rochester, N. Y.

ST. LOUIS COUNTY MEDICAL SOCIETY, SECTION OF EYE, EAR,  
 NOSE AND THROAT

President: Dr. Orien B. Patch, 205 West 2nd St., Duluth, Minn.  
 Secretary: Dr. J. C. O'Neill, 205 West 2nd St., Duluth, Minn.  
 Place: St. Mary's Hospital, Duluth. Time: Second Thursday of each month from September through May.

ST. LOUIS OPHTHALMIC SOCIETY

President: Dr. Daniel Bisno, 4500 Olive Street, St. Louis 8.  
 Secretary: Dr. J. H. Bryan, 3720 Washington Blvd., St. Louis 8.  
 Place: Elliott Auditorium, McMillan Hospital. Time: Fourth Friday of each month from October to April, inclusive, except December, at 8:00 p. m.

SAN ANTONIO SOCIETY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

President: Dr. A. A. Nesbit, South Texas Bank Bldg., San Antonio, Texas.  
 Secretary-Treasurer: Dr. Fred B. Cooper, 827 Medical Arts Bldg., San Antonio 5, Texas.  
 Place: San Antonio, Texas, Brooke General Hospital and Randolph Field. Time: 7 p. m., second Tuesday of each month from October to May.

SAN FRANCISCO COUNTY MEDICAL SOCIETY, SECTION ON EYE,  
 EAR, NOSE AND THROAT

President: Dr. William Duggan, 490 Post St., San Francisco 2.  
 Secretary: Dr. George Campion, 490 Post St., San Francisco 2.  
 Place: Society's Bldg., 2180 Washington St., San Francisco 9. Time: 8:15 p. m., fourth Tuesday of every month except June, July and December.

SHREVEPORT EYE, EAR, NOSE AND THROAT SOCIETY

President: Dr. Ralph Riggs, Medical Arts Bldg., Shreveport, La.  
 Secretary-Treasurer: Dr. Frank L. Bryant, 2622 Greenwood Rd., Shreveport 2, La.  
 Place: Shreveport Club. Time: 6:30 p. m., first Monday of every month except June, July and August.

## SPOKANE ACADEMY OF OPHTHALMOLOGY AND OTO-LARYNGOLOGY

President: Dr. Phillip B. Greene, Old National Bank Bldg., Spokane, Wash.  
Secretary: Dr. Cornelius E. Hagan Jr., Old National Bank Bldg., Spokane, Wash.  
Place: Paulsen Medical and Dental Bldg. Time: 8 p. m., fourth Tuesday of each month except, June, July and August.

## TOLEDO EYE, EAR, NOSE AND THROAT SOCIETY

President: Dr. James Cooper, 316 Michigan Street, Toledo 2, Ohio.  
Secretary: Dr. William H. Bonser, 219 15th Street, Toledo, Ohio.  
Place: Toledo Club. Time: 8:00 p. m., second Tuesday of each month.

## TORONTO ACADEMY OF MEDICINE, SECTION OF OPHTHALMOLOGY

Chairman: Dr. A. L. Morgan, Medical Arts Bldg., Toronto, Canada.  
Secretary: Dr. J. C. Hill, Medical Arts Bldg., Toronto 5, Canada.  
Place: Academy of Medicine, 288 Bloor St. W. Time: 8:00 p. m., second Tuesday of each month, November to April.

## WASHINGTON, D. C., OPHTHALMOLOGICAL SOCIETY

President: Dr. Jerome A. Sansoucy, 2017 Massachusetts Ave. N. W., Washington, D. C.  
Secretary: Dr. Thomas A. Egan, 1835 Eye St. N. W., Washington, D. C.  
Place: Hotel Kennedy-Warren. Time: 6:00 p. m., first Monday of November, January, March and May.

## WILKES-BARRE OPHTHALMOLOGICAL SOCIETY

President: Dr. Joseph V. Connoles, 72 W. Union Street, Wilkes-Barre, Pa.  
Secretary: Dr. Samuel T. Buckman, 70 S. Franklin St., Wilkes-Barre, Pa.  
Place: Luzerne County Medical Society. Time: 8:30 p. m., last Tuesday of each month from October to May.

## HEREDITY AND RETINOBLASTOMA

ALGERNON B. REESE, M.D.  
NEW YORK

IT HAS been well established that there is a strong hereditary tendency in retinoblastoma. Although the exact way in which the disease is transmitted has not been agreed on, evidence largely points to its being a dominant trait irregular in type. Some cases have been reported of collateral involvement in siblings whose parents were apparently normal, and many cases of direct transmission from parent to child.

There remains, however, the majority of cases in which the appearance of the neoplasm seems to be sporadic, no relative of the child having had the disease and the parents both having normal eyes. This sporadic type may be a somatic mutation arising from a developmental disturbance, but it must be borne in mind that should such a case be arrested the patient might well found a fraternity in which the growth would become a dominant trait.

Two questions of genetic interest in relation to retinoblastoma are frequently posed the ophthalmologist. First, when retinoblastoma has occurred in one child of healthy parents, what is the likelihood that further siblings will be affected? Second, is it advisable for the adult survivor of retinoblastoma to have children?

Many instances of the hereditary and familial occurrence of retinoblastoma have been documented in ophthalmic literature. Extensive bibliography on the subject can be found in the papers of Benedict,<sup>1</sup> Rados,<sup>2</sup> Weller,<sup>3</sup> Griffith and Sorsby,<sup>4</sup> and Falls.<sup>5</sup> Although reported

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From the Institute of Ophthalmology of the Presbyterian Hospital and Memorial Center for the Treatment of Cancer and Allied Disease.

1. Benedict, W. L.: Retinoblastoma in Homologous Eyes of Identical Twins, *Arch. Opth.* 2:545 (Nov.) 1929.

2. Rados, A.: Occurrence of Glioma of Retina and Brain in Collateral Lines in Same Family, *Arch. Opth.* 35:1 (Jan.) 1946.

3. Weller, C. V.: The Inheritance of Retinoblastoma and Its Relationship to Practical Eugenics, *Cancer Research* 1:517, 1941.

4. Griffith, A. D., and Sorsby, A.: The Genetics of Retinoblastoma, *Brit. J. Opth.* 28:279, 1944.

5. Falls, H. F.: Inheritance of Retinoblastoma (Two Families Supplying Evidence), *J. A. M. A.* 133:171 (Jan. 18) 1947.

pedigrees definitely indicate a hereditary tendency, a mere tendency to a disease which is reputed to occur only once in 34,000 births may not be important. The literature on the subject concerns itself mostly with isolated cases which unquestionably show the hereditary trend but which are not adequate for statistics on incidence.

#### PRESENT STUDY

We communicated concerning 171 consecutive cases of retinoblastoma encountered at the Institute of Ophthalmology and the Memorial Center for the Treatment of Cancer and Allied Diseases. We were successful in receiving the desired data on 91 cases.

#### *Series of Sporadic Cases, Showing Number of Siblings Involved*

Author	No. of Cases	Instances of More Than One Sibling	Total No. of Children
Lawford, J. B., and Collins, E. T.: Roy. London Ophth. Hosp. Rep. 13:12, 1890-1893.....	60	0	...
Marshall, C. D.: Roy. London Ophth. Hosp. Rep. 14:456, 1895-1897.....	32	1	...
Owen, S. A.: Roy. London Ophth. Hosp. Rep. 16:323, 1905-1906..	52	1	...
Adam, C.: Ztschr. f. Augenh. 25:330, 1911.....	44	3	...
Berrisford, R. D.: Roy. London Ophth. Hosp. Rep. 20:296, 1915-1917.....	41	0	...
Davenport, R. C.: Brit. J. Ophth. 10:474, 1926.....	27	0	...
Hemmes <sup>7</sup> .....	48	0	211
von Heijl, C.: Aeta Ophth. 12:69, 1934.....	60	0	...
Stoek, W.: Ber. ü. d. Versamml. d. deutsch. ophth. Gesellseh. 51:106, 1936.....	28	0	...
Reiser <sup>6</sup> .....	16	0	64
Keller, P.: Arch. d'opht. 2:813, 1938.....	13	0	...
Lange, H.: Klin. Monatsbl. f. Augenh. 10:854, 1938.....	35	0	...
Griffith and Sorsby <sup>4</sup> .....	53	1	...
Our series.....	86	1	103
Total.....	605	7	378

Eighty-six cases were sporadic (cases in which both parents were healthy) and 5 cases were collateral (the patients were the progeny of parents one of whom was a retinoblastoma survivor).

*Sporadic Cases.*—For 60 of the 86 sporadic cases the siblings totaled 103. Only 1 sibling of these 103 had retinoblastoma. There are a number of large series of sporadic cases in the literature, and the data on some of them, including our own, are shown in the table. It can be seen that of 605 sporadic cases there were 7 in which siblings were affected. However, because the total number of siblings was indicated only in three series (those of Reiser,<sup>6</sup> Hemmes<sup>7</sup> and ours), percentages on the likelihood of the occurrence of retinoblastoma in siblings

6. Reiser, K. A.: Bemerkungen zur Erblchkeitsfrage beim Glioma retinae, Klin. Monatsbl. f. Augenh. 99:350, 1937.

7. Hemmes, G. D.: Untersuchung nach dem Vorkommen von Glioma retinae bei Verwandten von mit dieser Krankheit behafteten, Klin. Monatsbl. f. Augenh. 86:331, 1931.

must be based entirely on these three series, which together comprise 150 cases in children, who had a total of 378 siblings. Among these siblings there was only 1 case of retinoblastoma, making the incidence less than 2.9 in 1,000. Analysis of the data in our series by the method of the confidence range indicates that if 1 of 103 siblings had retinoblastoma there is a 95 per cent likelihood that the true range lies between zero and 4 per cent of siblings of patients with retinoblastoma born of healthy parents. The use of the total of 378 siblings (in the three series) would, of course, yield a considerably lower confidence range. An analysis, therefore, of several series of unselected cases of sporadic retinoblastoma indicates that the likelihood that a second sibling will be affected is less than 4 per cent, and is probably nearer 1 per cent. I do not hesitate, therefore, to advise healthy parents who have had one child with retinoblastoma to have more children.

*Collateral Cases.*—No statistical analysis has been made of any appreciable number of parents who have themselves survived retinoblastoma, and therefore an accurate measure of the likelihood of transmission of the disease from a surviving parent to a child is not possible.

Reiser <sup>6</sup> in 1937 indicated that of thousands of cases, with an approximate survival rate of about 50 per cent, there were probably hundreds in which the patient reached the reproductive age, but at that time only 20 to 25 cases of verified transmission had been reported. He stated, therefore, that the transmission rate was not high enough to warrant the sterilization of retinoblastoma survivors.

However, in our experience with retinoblastoma we have had 5 instances in which the progeny of survivors of retinoblastoma had retinoblastoma. These were briefly as follows:

CASE 1 (N. D.).—The father had had both eyes enucleated in infancy because of retinoblastoma. His only child had bilateral retinoblastoma, and bilateral enucleation was done. The child survived and is now 10 years old.

CASE 2 (M. S. D.).—The father had bilateral retinoblastoma and bilateral enucleation in infancy. He was told that it would be safe to have children. The first child had bilateral retinoblastoma, for which bilateral enucleation was done, and she now survives, after eight years. Before the fate of the first child was known, a second child was conceived. This child also had bilateral retinoblastoma, for which an enucleation of the eye with the more advanced lesion was done. The fellow eye was treated with roentgen radiation.

CASE 3 (M. J. C.).—The father had an eye enucleated in infancy because of a tumor (presumably a retinoblastoma). His first child died of retinoblastoma. The second child is living and well. The third child had bilateral retinoblastoma. One eye had to be enucleated, and the other was treated by irradiation.

CASE 4 (C. G. and M. G.).—The father had one eye enucleated in infancy because of retinoblastoma. His first child had bilateral retinoblastoma. One eye was enucleated, and the other was treated with roentgen radiation. His second



child also had bilateral retinoblastoma. Because of the advanced stage of the tumor, both eyes had to be enucleated.

CASE 5 (R. V.).—The mother had one eye enucleated at the age of 2 years. Her only daughter had bilateral retinoblastoma. The child died because of intracerebral extension of the tumor.

We have in our series of 184 cases of retinoblastoma only 5 survivors with children. The children total 8, and 7 of these had bilateral retinoblastoma. These figures are sufficiently impressive to me to interdict the bearing of progeny by all survivors of retinoblastoma.

#### CONCLUSIONS

1. There is no contraindication to healthy parents who have had one child with retinoblastoma having more children.
2. A survivor of retinoblastoma should not have children.

73 East Seventy-First Street.

# CONTINUOUS INTRAVENOUS INJECTION OF TYPHOID VACCINE IN TREATMENT OF CERTAIN OPHTHALMIC DISEASES

JOHN J. CURRY, M.D.

AND

ELMER A. SHAW, M.D.

BOSTON

FOR MANY years artificial fever, induced in the hypertherm cabinet or by single injections of foreign protein or typhoid vaccine, has been used in the treatment of various diseases of the eye. In the past decade attention has been directed particularly toward the use of single, rapid intravenous injections of typhoid vaccine. A drawback of this type of therapy is the unpredictable febrile reaction. In some cases extremely severe chills and high fever occur, whereas in others several injections are required, over a period of days, before the proper degree of fever is secured. Moreover, typhoid therapy is frequently withheld from elderly patients or persons with heart disease because of the risk entailed in a severe reaction. Solomon and Somkin<sup>1</sup> in 1942 introduced the method of controlled hyperpyrexia by the continuous intravenous administration of typhoid vaccine. It occurred to us that this type of therapy might well be applied to the treatment of certain ophthalmic diseases.

## MATERIALS AND METHODS

One cubic centimeter of typhoid vaccine in a concentration of 1,000,000,000 killed organisms per cubic centimeter was suspended in 1 liter of sterile isotonic sodium chloride solution U. S. P. With the patient recumbent in bed, a 21 gage intravenous needle was inserted in an antecubital vein and the mixture allowed to flow at a rate of 20 to 30 drops per minute. Rectal temperatures were recorded at fifteen minute intervals. If the temperature did not begin to rise in thirty to forty-five minutes, the rate of flow was doubled. On the other hand, if the rise in temperature was rapid, the rate of flow was decreased. The degree of fever desired varied from case to case, depending on the condition under treatment and the physical condition of the patient. In aged or debilitated patients and in those with notable arteriosclerosis, chilling and hyperpyrexia were avoided by

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From the Robert Dawson Evans Memorial and the Ophthalmologic Service, Massachusetts Memorial Hospitals.

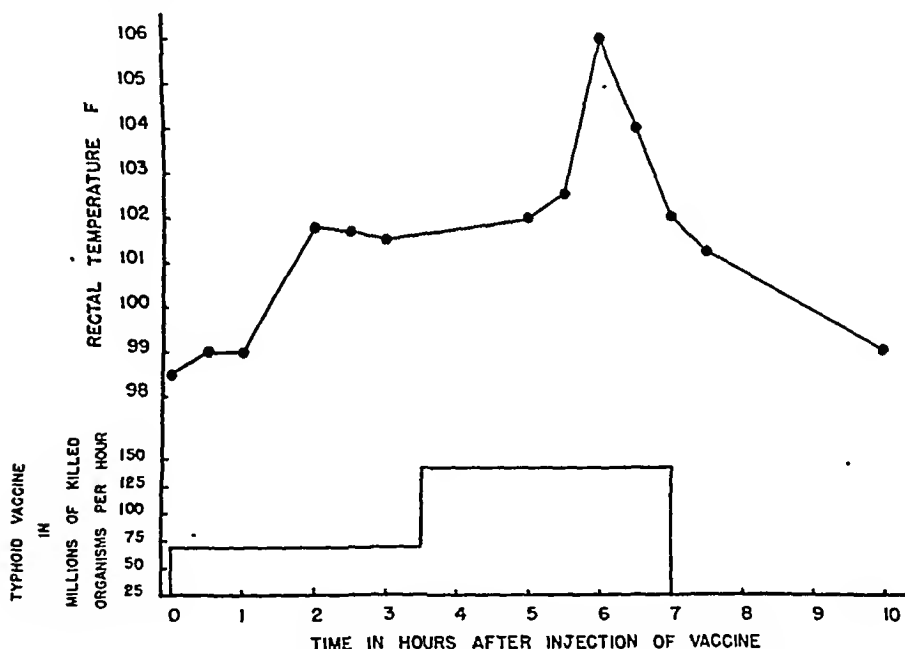
1. Solomon, H. A., and Somkin, E.: An Improved Method of Obtaining Sustained Controlled Hyperpyrexia with Triple Typhoid Vaccine, *Am. J. M. Sc.* 203:736, 1942.

using very slow rates of infusion. With other patients, those with syphilitic keratitis, for example, it seemed desirable to have a temperature over 102 F., and preferably over 104 F., for several hours.

If improvement was not pronounced within forty-eight hours after treatment, a not uncommon occurrence, a second continuous injection of typhoid vaccine was given. With the second course of therapy the rate of flow was frequently more rapid. When the patient was subjected to sustained hyperpyrexia, from 50 to 100 mg. of meperidine hydrochloride (demerol hydrochloride®) was given intramuscularly prior to the administration of the typhoid vaccine. The only other medication employed was local instillation of atropine sulfate ointment.

### RESULTS

Fourteen patients with nonspecific iritis were given continuous intravenous injections of typhoid vaccine over periods of four to twelve hours. Eight patients required only one course of therapy. Of these,



Correlation of temperature response and administration of typhoid vaccine (patient S. K.).

2 showed pronounced to complete improvement in twenty-four hours, whereas the other 6 required forty-eight hours to attain a similar result.

Patient S. K., of this group of 8 patients, was especially interesting because despite two single intravenous injections of typhoid vaccine an increased exudate in the anterior chamber occurred and the condition of the eye became worse. However, within twenty-four hours after a single course of continuous typhoid vaccine therapy, with about eight hours of fever and a maximum temperature (rectal) of 106 F. (figure), the exudate cleared and the eye became much whiter. The remaining 6 patients required a second course of therapy because

improvement was not satisfactory. Within forty-eight hours after the second injection, however, all the patients had shown pronounced to complete improvement.

In 4 of the 14 patients with iritis, because of debility and age or disease of the coronary arteries, the typhoid vaccine in sodium chloride solution was given very slowly, so that no chilling occurred and the temperature did not rise above 102 F. (rectal). Two of these patients required an additional course of therapy, but, so far as could be determined, in this small group, improvement was just as prompt as in the patients treated with prolonged high fever.

Two patients with suspected sympathetic ophthalmia were given continuous intravenous therapy of typhoid vaccine; the first patient showed clearing within twenty-four hours after one course of therapy, whereas the second required two courses.

In 1 patient with syphilitic keratitis two bouts of fever were induced, a total of nine hours with a temperature over 103.6 F. (rectal). Clearing took place within forty-eight hours of the second course of therapy.

#### COMMENT

While little is definitely known concerning the mechanism of improvement following the administration of typhoid vaccine, it has generally been assumed that the degree of fever is the important factor. Indeed, this belief has led to the widespread use of the hypertherm cabinet. However, the results of therapy in some of our patients, in whom very slight fever was induced, indicate that fever may not be the only important factor.

In any event, the continuous intravenous administration of typhoid vaccine appears to be superior to single injections of typhoid vaccine because the results are predictable and the degree of fever and chilling may be controlled. This type of therapy may be given safely to elderly and debilitated patients and to persons with coronary arteriosclerosis. A disadvantage is that intravenous drip apparatus is necessary and the administration of the vaccine must be carefully supervised.

#### SUMMARY

A total of 17 patients with ophthalmic diseases, including non-specific iritis, syphilitic keratitis and suspected sympathetic ophthalmia, were treated by the continuous intravenous administration of typhoid vaccine, with gratifying results in every case. This method of treatment is recommended because it may be given safely to elderly and debilitated patients and the degree of fever and chilling may be controlled.

Massachusetts Memorial Hospitals.

## MINIMAL DEFECTS IN VISUAL FIELD STUDIES

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NEW YORK

**I**NTRACRANIAL lesions that interfere with the visual pathways will cause defects in the visual fields, the extent depending on the amount of interference. When such interference is great enough, the field defect produced is correspondingly large and is easily elicited with routine perimetric studies and even by confrontation. Since the presence of field defects is often an important means of localizing, lateralizing or even recognizing the presence of an intracranial lesion, it is important to be able to detect any defect in the visual field, however small. Such small defects are often difficult to detect and the recognition of some of them will be discussed in the present paper.

In order to recognize minimal defects, one must use minimal stimuli for the various isopters being tested. In other words, if one wishes to explore a certain part of the field for slight defects, one must use the smallest stimulus which is normally known to be just recognized in this particular arc of the field.

For minimal peripheral defects, a 5/330 or 3/330 test object may be used. However, it has been my experience that a 1/330 test object will often bring out a defect that will be missed with a 5/330, a 3/330 or even a 2/330 test object, and at the Montefiore Hospital the 1/330 test object has, therefore, become a favorite for detecting minimal defects in the peripheral field. For the recognition of early or minimal defects in the more central isopters, the 1/2,000 test object is a good minimal stimulus to use. This test object, if used to full advantage, can usually be made to bring out the most central and minimal defects, although one can supplement such delicate testing with 0.5/2,000 white and 2/2,000 red for the inner 2 degrees of field for lesser defects, if necessary.

For practical purposes, therefore, the 1/330 test object has been used for study of the peripheral fields and the 1/2,000 test object for study of the central fields in order to detect minimal defects.

In using these minimal stimuli, if one merely brings the test object along the various meridians and records the readings mechanically,

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Read before the Section of Ophthalmology, New York Academy of Medicine, April 19, 1948.

From the Ophthalmological Service of Dr. Samuel Gartner and the Neurosurgical Service of Dr. Leo M. Davidoff, Montefiore Hospital for Chronic Diseases.

one is apt to miss small defects. Rather, the technic must be guided by the clinical features of the case, as an indication of what to look for. One of the commonest features sought in interference due to intracranial lesions is incomplete hemianopsia, whether homonymous, temporal or bitemporal. In order to recognize such early hemianoptic

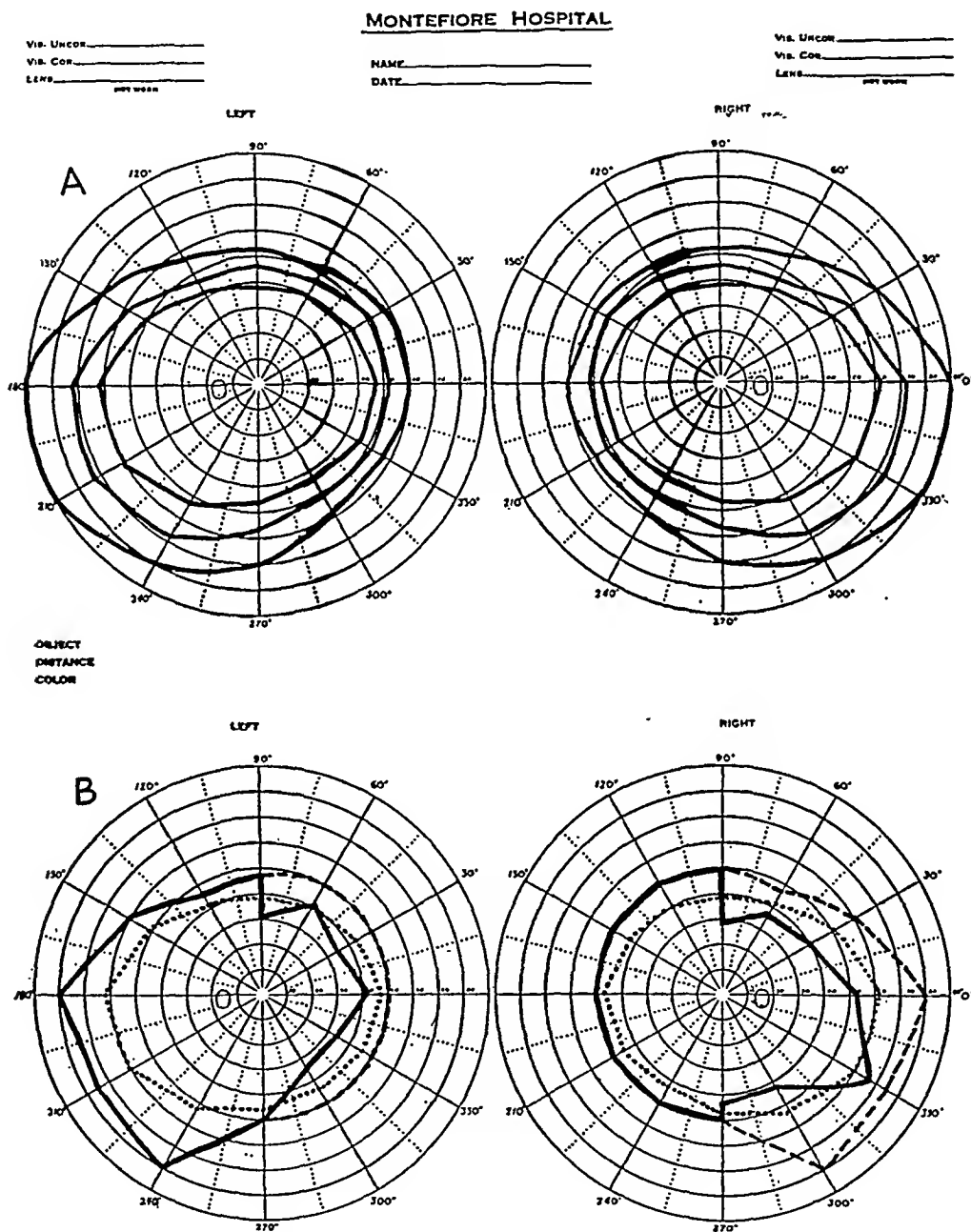


Fig. 1.—*A*, Montefiore chart for peripheral fields. The isopters for 5.8/330, 3/330 and 1/330 white are shown. These isopters are actually represented by pale green lines, which to the casual glance are barely perceptible against the white paper and the accompanying deep orange meridional and arc markings. For purposes of this photograph, the isopter lines have been accentuated with black ink.

*B*, right homonymous hemianoptic defect, as shown by level differences and breadth of field. The explanation of these lines will be found in the text of this article.

defects, I use three sets of criteria in examination and interpretation: (1) level differences, (2) rapid comparisons for qualitative differences, and (3) breadth of field.

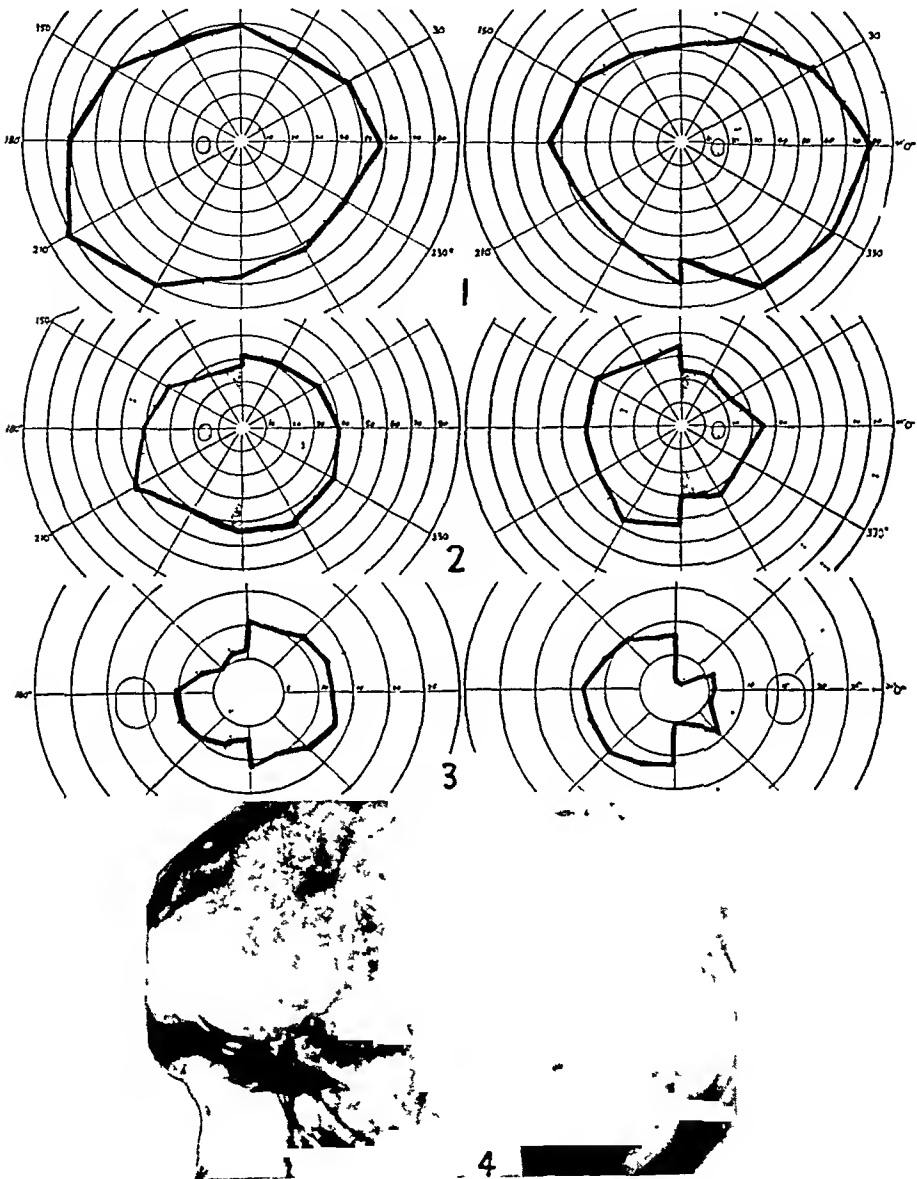


Fig. 2 (case of adenoma of the pituitary gland).—1, practically normal fields for 3/330 white except for a single level difference in the 270 degree meridian of the right eye. 2, peripheral field for 1/330 white, showing qualitative defect on the temporal side of all the vertical meridians. This defect was elicited by rapid comparisons and is indicated by stippling in those areas. The left eye also shows a small level difference in the 90 degree meridian. Larger level differences are seen in both vertical meridians of the right eye. 3, bitemporal field defect for 1/2,000 white. These defects are no longer minimal. 4, large, eroded sella turcica.

All these field studies were made at the same examination

## LEVEL DIFFERENCES

By level differences, I refer to slight differences of extent of field on the left and the right sides of the vertical meridians, giving a step-like appearance to the field of vision at the vertical meridians. These

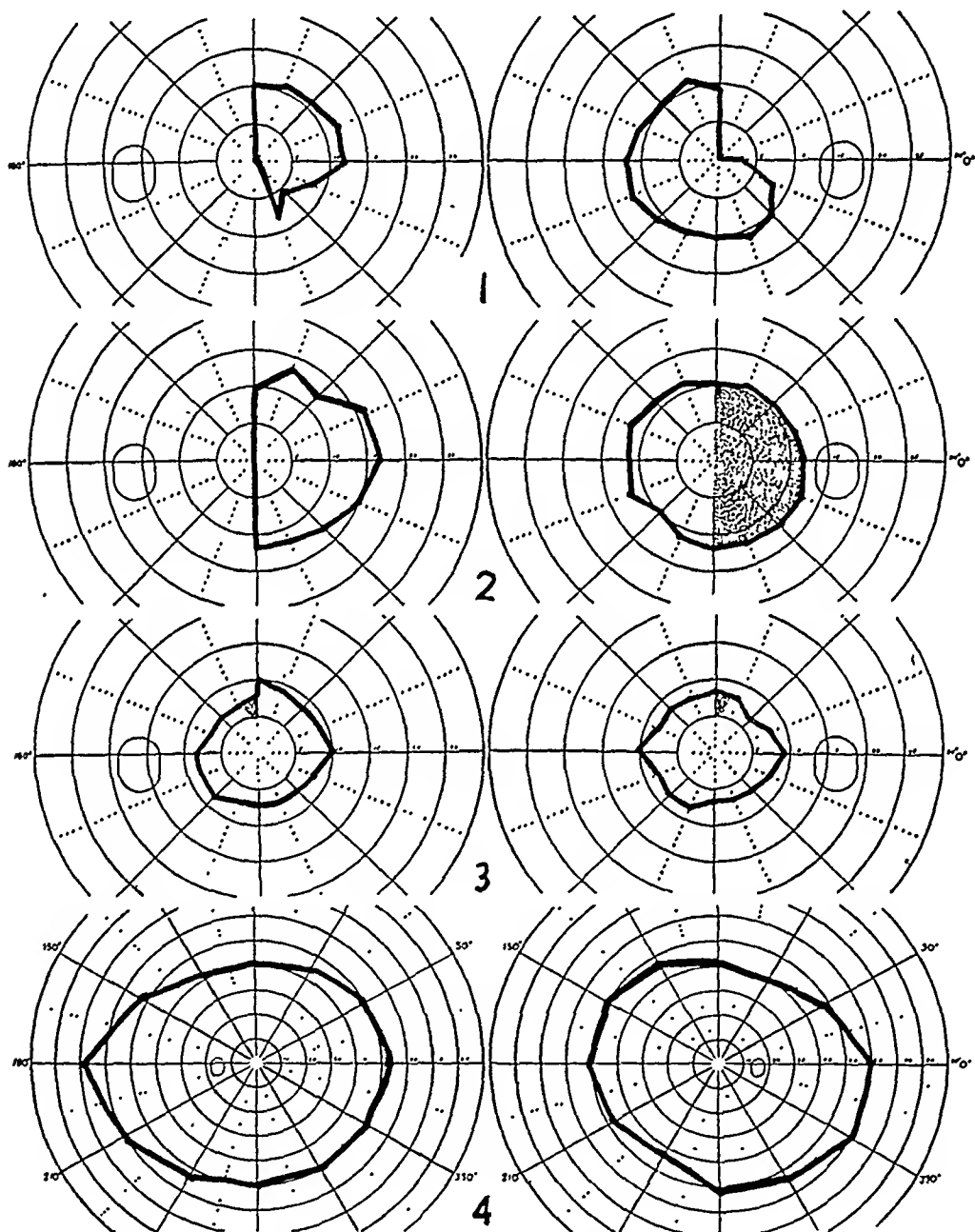


Fig. 3 (case of adenoma of the pituitary gland).—1, preoperative field for 1/2,000 white, showing bitemporal hemianoptic defect. 2, 1/2,000 fields on the eighth postoperative day. The left eye shows a return of the lower nasal field with improvement of visual acuity from 15/40 to 15/15. The right eye shows a return of temporal field, although of a relative nature. The relative quality of this temporal field was brought out by rapid comparisons. 3, field for 1/2,000 three months after operation. The left eye still shows some level difference and qualitative difference brought out by rapid comparisons. The right eye shows only a qualitative difference above. 4, peripheral field for 1/330 white, taken at the same time as the fields in 3, showing absence of any defect.



differences may be as little as 5 degrees on the perimeter and only 2 degrees on the 2 meter screen. Some observers may believe that such small differences are within the limits of error in technic. However,

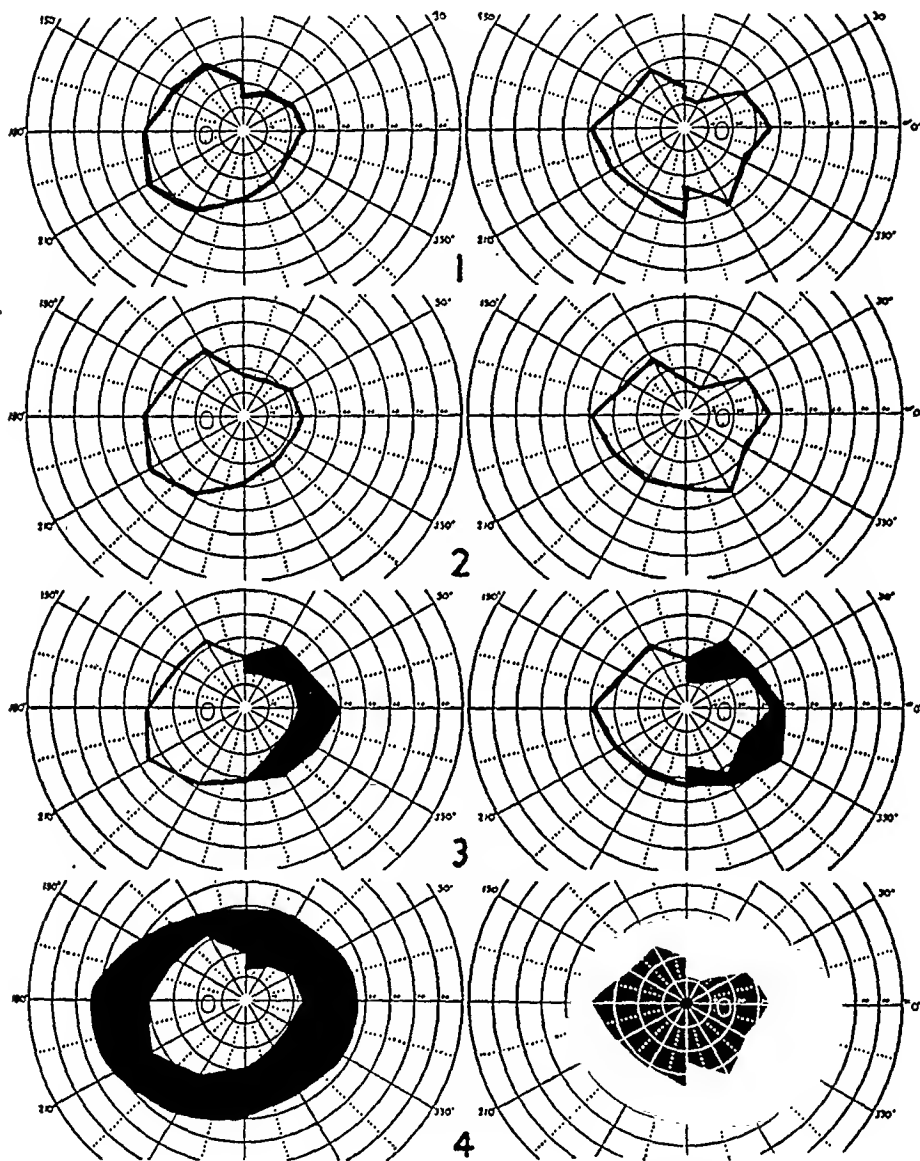
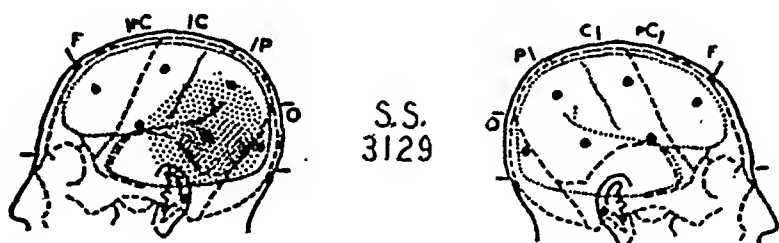


Fig. 4 (case of meningeoma of the left temporoparietal area).—1, peripheral fields for 1/330 white, showing level differences. 2, the same fields plotted in the usual way without bringing out level differences. Such fields, on casual examination, may pass as showing only generalized peripheral contraction. Actually, even these fields show a right homonymous defect on comparison of the two nasal fields and the two temporal fields. 3, a larger temporal field in the left eye and a larger nasal field in the right eye, as evident from measuring breadth of field. When these larger half-fields are used as normals, the plotted fields show a right homonymous defect. 4, picture produced by actual plotting of these fields on the Montefiore chart and filling in to the appropriate isopter. These fields demonstrate the right homonymous defect determined both by level differences and by breadth of field. In addition, they show a generalized peripheral contraction, undoubtedly due to prolonged intracranial pressure.

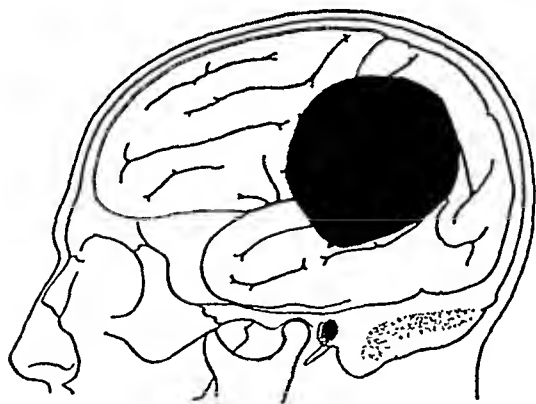
if consistently found, they must be considered significant. The side of the lesser reading is likely to be that of a defective hemianoptic field. In eliciting these level differences, one must test the field on each side of the vertical meridian independently and make the recordings for the nasal and the temporal side separately. These recordings are placed on the vertical meridian of the chart and connected by a straight line, the upper and lower ends of which will subsequently be connected



FAIRLY WELL DEMARCATED E.E.G. ABNORMALITY.  
CONCENTRATION OF DISTURBANCES.

APPARENTLY SECONDARY ANTERIOR EFFECTS NOT PORTRAYED.

1



2

Fig. 5.—Additional clinical data in the case the fields of which are shown in figure 4. 1, area of disturbance as determined by electroencephalography. 2, surgeon's sketch, showing site of tumor as found on operation.

with the proper points found on the adjoining nasal and temporal meridians.

In figures 1B, 2, 3, 4, 6, 7 and 9, there are fields showing the small but constant level differences on the nasal and the temporal side of the vertical meridians. If these level differences had not been looked for and recorded, the fields could easily assume a rather normal-looking pattern and pass as normal to the inexperienced eye.

For example, in figure 6, 1 illustrates the actual field found by determining the level differences in the vertical meridians; 2 in the same figure shows what the field would look like if one had explored the vertical meridians merely along the center of the perimeter arc, without bothering to explore each side of the vertical meridian separately. Similar examples are shown in figures 4, 7 and 9.

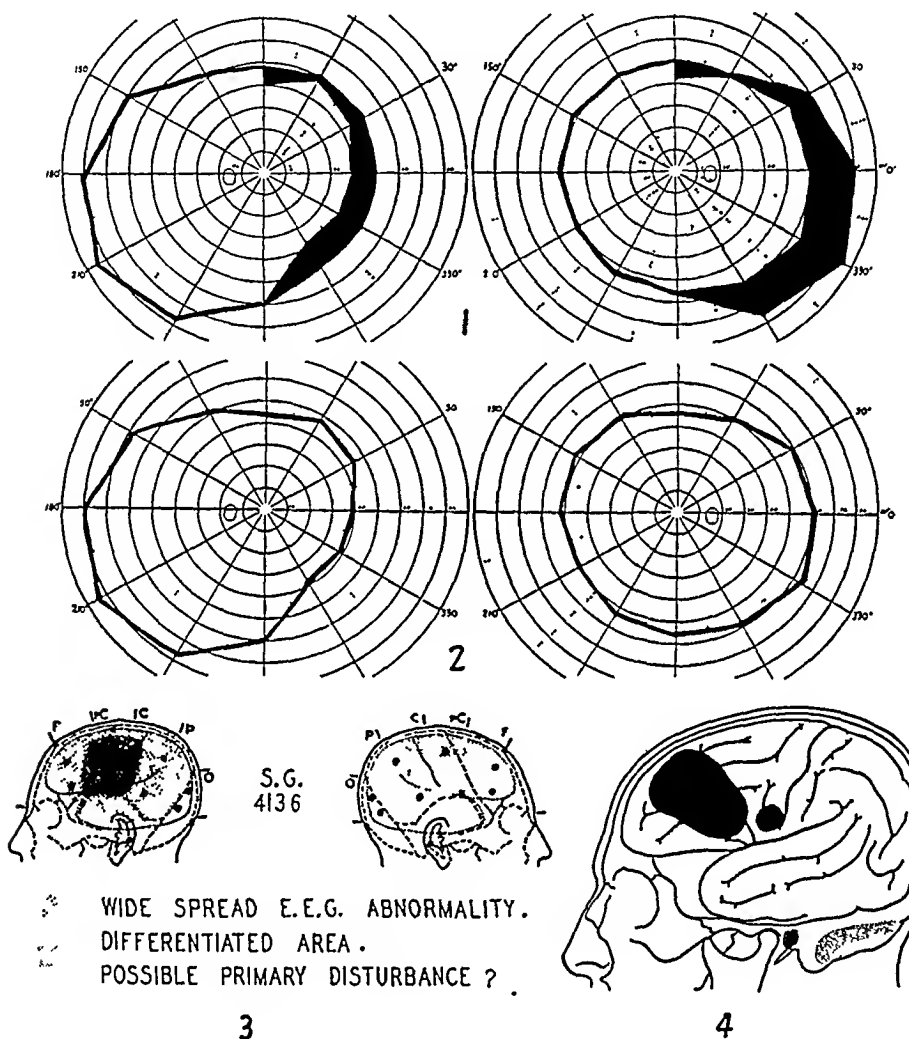


Fig. 6 (case of metastatic tumor involving an area of the left cerebrum, but showing only minimal interference with visual pathways).—1, fields filled in, showing minimal right homonymous hemianoptic defect, determined both by level differences and by breadth of field 2, same fields plotted without measurement of level differences. The rounded right peripheral field should lead the examiners to suspect a temporal peripheral defect. 3, areas of abnormality as determined by electroencephalography. 4, surgeon's postoperative sketch, showing the most apparent area of the mass.

In testing on either side of the vertical meridians of the perimeter or the tangent screen, one should keep well away from the meridian

proper, especially if fixation is not very good. The more reliable the patient and his fixation, the closer the examiner dares to bring the test object to the 90 degree or the 270 degree meridian on each side. With the narrow perimeter arcs, one may start moving the test object very well near the edge of the perimeter arc peripherally and bring it in radially toward fixation. With the wider perimeter arcs, such as the Brombach, one must stay farther in from the edge since the

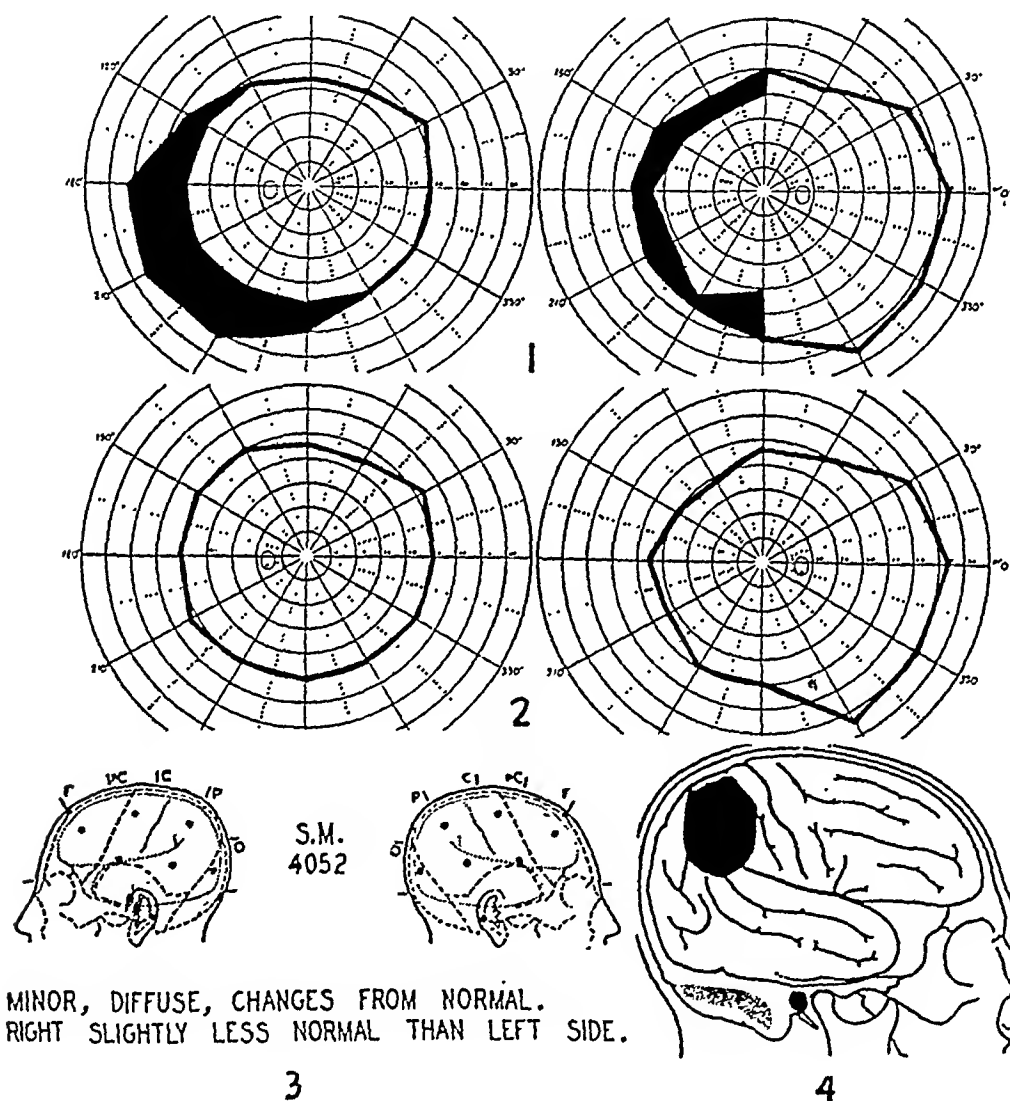


Fig. 7 (case of tumor in right parieto-occipital area).—In this case, prior to air studies, there was a question of lateralization. 1, peripheral fields for 2/330 white, showing left homonymous hemianoptic defect, both by level differences and by breadth of field. 2, fields as plotted without level differences. These fields might easily pass as normal to casual observation. However, the rounded left peripheral field should arouse suspicion of a temporal defect. Even in this plotting, the left homonymous hemianoptic defect may be recognized by comparing the breadth of field in the corresponding halves of the two eyes. 3, results of electroencephalography, showing only very little disturbance, without definite localization. 4, surgeon's postoperative sketch, showing location of tumor on the right side.

width of the perimeter is such that one would actually be testing about 10 degrees off the vertical meridian near the periphery.

Even though these level differences are very small, if they are constant and form the picture of a definite field defect that is in keeping with the rest of the clinical picture, one may feel quite sure of their significance. A definite level difference in the 90 degree meridian for the 1/2,000 test object may be the first evidence of a beginning temporal defect due to chiasmal interference.

#### RAPID COMPARISONS FOR QUALITATIVE DIFFERENCES

This method makes use of a single test object to examine different parts of the field in which it is seen for small amounts of defect. Thus, while the 1 mm. white test object may be recognized throughout all the 15 or 20 degrees of field on the 2 meter screen, by rapidly shifting



Fig. 8.—Roentgenograms in the case fields for which are shown in figure 7. 1, right lateral ventricle, smaller and pressed down as by a mass from above; 2, lateral view, showing smaller right ventricle being pressed down from above and behind.

the test object from the nasal to the temporal side of the vertical meridian, at comparable levels and distances from the meridian, where visual acuity should normally be the same on the two sides, one may be told by the patient that the test object is definitely much clearer and more definite on one side than on the other. This difference may be considered a relative defect for that particular visual angle on the side of poorer vision and as corroboration of the existence of a hemianoptic defect. Similarly, a minimal defect in the cecocentral area of optic neuritis may be brought out by rapidly comparing the perception of the test object on the horizontal meridian in the cecocentral area with its visibility a little higher up or lower down. Also, a relatively mild Bjerrum scotoma may be picked up by bringing out

a definite difference in perception above and below the nasal horizontal meridian. In all these conditions, if the defective area is not very dense, merely bringing the test object along slowly from good field to poor field, or vice versa, will not bring out the small defect, while by suddenly displaying it in good field and rapidly changing it to poor field one will bring out the difference quite readily, even though it is a small one. I use this method of rapid comparisons routinely with the 1/330 as well as the 1/2,000 test whenever I examine the vertical meridians for hemianoptic defects.

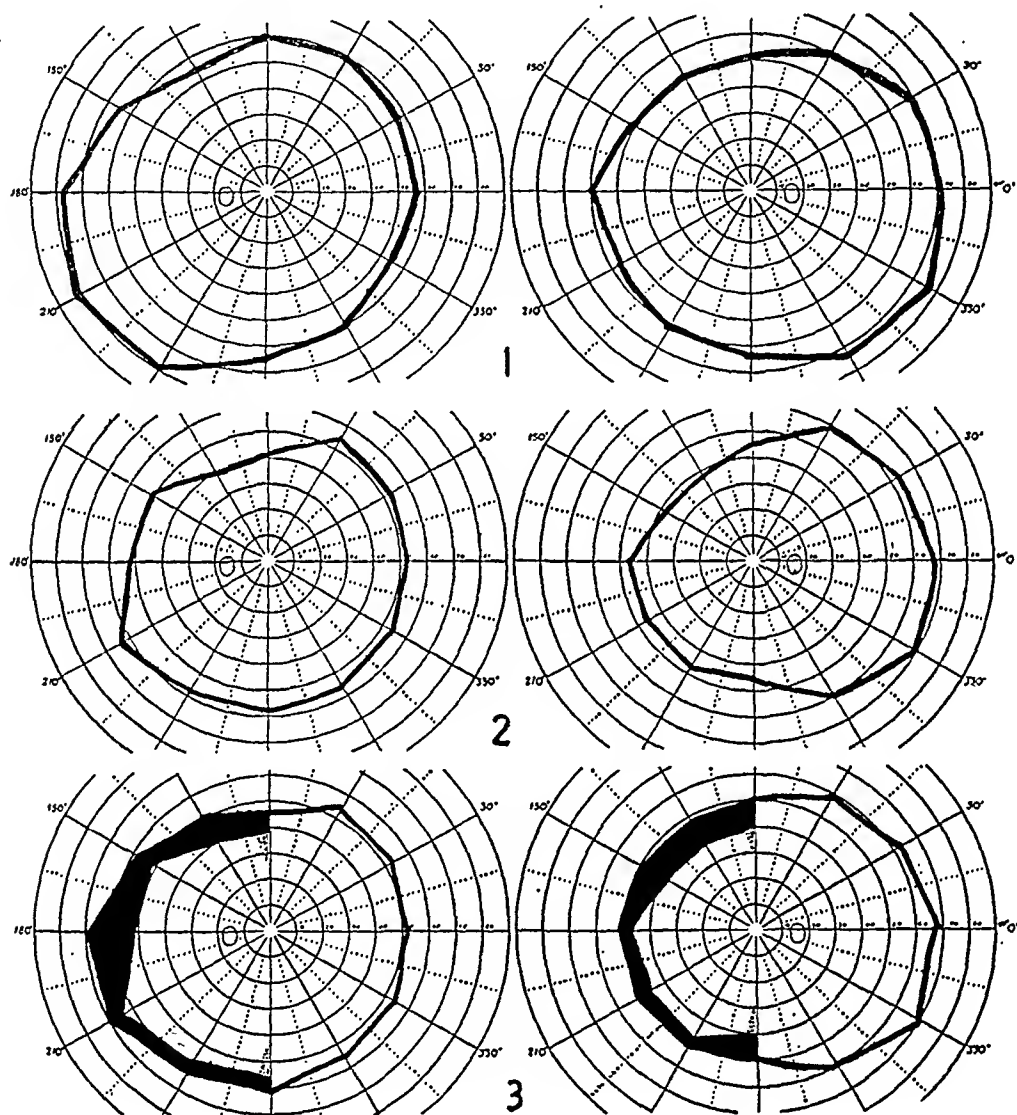
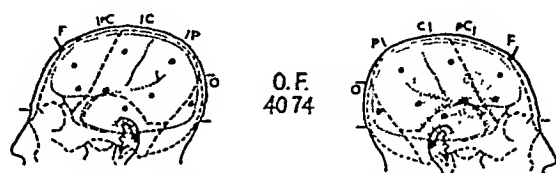


Fig. 9 (case of meningioma of the right frontotemporal area).—1, peripheral fields for 2/330 white. Although looked for, no level differences could be found with this visual angle. 2, peripheral fields for 1/330 white, plotted without effort to obtain level differences. These fields may pass as not remarkable on casual inspection. However, comparison of corresponding halves for breadth of field reveals definite left homonymous defect. 3, peripheral fields for 1/330 white showing level differences and differences in breadth of field, both pointing to a left homonymous hemianoptic defect. In addition, rapid comparisons corroborated these findings. In all four vertical meridians, at the periphery, the patient saw the test object less clearly on the left side than on the right. This is indicated by the stippling in the defective areas.

Besides the 1/330 and the 1/2,000 white, a good test object for rapid comparisons is the 5/2,000 red. Often, this test object will be called "red" in the good field and "pink" in the other, or, in poor fields, "pink" on one side and "grayish" on the other.

In using rapid comparisons on the perimeter, it is well to bring the test object in 5 or 10 degrees from the periphery of the field before alternating the test object in the two areas being compared. This has the advantage that better fields are compared than the very poor fields at the extreme periphery. An example of information brought

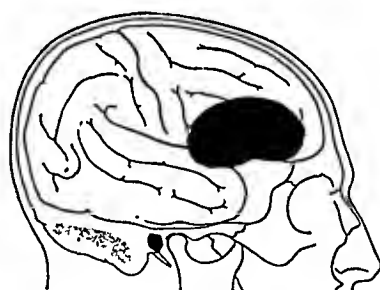


E.E.G. ABNORMALITY.  
MAXIMAL DISTURBANCE.

1



2



3

Fig. 10 (additional clinical data in case fields of which appear in figure 9). —1, area of greatest disturbance as determined by electroencephalography. 2, roentgenograms showing right lateral ventricle pushed over to the left side, apparently by a space-occupying mass on the right side. 3, surgeon's postoperative sketch, showing the right frontotemporal location of the tumor.

out by rapid comparisons is found in 2 of figure 2. Here, the 1/330 field for the left eye shows definitely worse vision on the temporal side of the 90 and 270 degree meridians, while there is no level difference below and only a slight one above. In the same figure, the 1/330 field for the right eye shows qualitative differences temporally near both vertical meridians, thus corroborating the larger level differences. These qualitative differences brought out by rapid com-

parisons corroborate the level differences and the resultant bitemporal hemianopsia. Another example of the use of "rapid comparisons" is seen in figure 3, 2. Here, four months after the removal of a pituitary tumor by Dr. Leo Davidoff, the level difference in the field of the right eye is no longer present, but when the 1 mm. test object was rapidly alternated from the nasal to the temporal side the patient persistently saw it as clearer on the left side (nasal) than on the right side (temporal), this difference being the only remaining evidence of the temporal hemianoptic defect present before operation. These areas of relatively poor vision are indicated on the charts by stippling and may be considered relative scotomas for the particular visual angle being used.

Of course, instead of this technic, one could use progressively smaller test objects until one found an object still visible in one part of the field but no longer in the other. This is often a lengthy and painstaking process and is not of real practical value. From a clinical point of view, the method of rapid comparisons is highly satisfactory, even though the exact amount of defect is not labeled accurately in terms of visual angle and absoluteness.

#### BREADTH OF FIELD

A third method of evaluating minimal field loss is by comparing the field with the normal field for the particular visual angle. The normal fields for the 5.8/330 and 1.0/330 test objects were carefully worked out by Ferree, Rand and Monroe<sup>1</sup> a number of years ago, and I have made use of their findings in designing the Montefiore chart showing the median normal isopters for three commonly used visual angles. This chart is shown in figure 1A. The three isopters marked off represent the median normal fields for 5.8/330, 3/330 and 1/330 white. I have discussed the use of this chart and method of filling in lost field in a recent article.<sup>2</sup> Depending on age and refractive error, contraction beyond these median normal isopters may be considered pathologic. However, in many cases the field plotted may be much larger than the accepted normal. In such cases, if the visual acuity and refractive error are approximately equal in the two eyes, one may reasonably expect the two nasal fields and the two temporal fields to be approximately equal in size, and I make use of this principle in computing loss of field. Therefore, if there is gross inequality in

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1. Ferree, C. E.; Rand, G., and Monroe, M. M.: Diagnostic Scales with the One Degree and 0.17 Degree Form Field Stimuli for Principal Meridional Quadrants Taken Separately, *Arch. Ophth.* 6:518 and 534 (Oct.) 1931.

2. Chamlin, M.: Recording of Visual Fields, *Am. J. Ophth.* 3:565 (May) 1948.



these corresponding fields, the smaller nasal field and the smaller temporal field may be considered defective.

Figure 1 *B* illustrates the method whereby I make use of this principle. Here, the heavy continuous line illustrates the field for 1/330 as actually found. The dotted line represents the median normal field for 1/330 white as found by Ferree, Rand and Monroe. It is obvious that the fuller temporal field of the left eye is not likely to have the small nasal field of the given normal as does its corresponding half. Rather, the normal nasal field for that person is likely to be correspondingly fuller than the median normal represented by the dotted line. Such a fuller nasal field may be assumed from the larger nasal field of the right eye, and it is seen that such a composite field is a more normal-looking peripheral field. Correspondingly, the normal temporal field of the right eye may be borrowed from the fuller temporal field of the left eye. These borrowed normal fields are shown in lines of dashes. In such cases, one may fill in the lost field up to the fuller normal fields of the patient's corresponding half-fields of the fellow eye, rather than up to the median normal fields of Ferree, Rand and Monroe. This principle is used in filling in the lost field in 3 of figure 9. Here, I made use of the patient's fuller half-fields in evaluating loss of breadth of field. Thus, breadth of field defects may be based on comparison with the normal fields as found by Ferree, Rand and Monroe, or on comparison with the fuller, corresponding halves of the patient's own fields.

It is interesting to note that in 2 of figure 7 the field of the left eye is almost perfectly round. Similarly, in 2 of figure 6 the field of the right eye is almost perfectly round. One should note that in both these fields there is actually some loss of temporal periphery; as a general rule, it is well to suspect an evenly rounded peripheral field as having a temporal defect. The normal peripheral field is more likely to be ovoid, with the larger diameter running from upper nasal to lower temporal field and the shortest diameter at right angles to it. This rule is unlike the one for the more central isopters, such as the field for 1/2,000 white, where one is more apt to find a rather evenly rounded, circular field normally.

Lately I have used the principle of simultaneous stimulation in eliciting level differences. Instead of using the small test object alternately on the two sides of the vertical meridian, two similar 1 mm. white test objects are passed along each side of the vertical meridian at the same time. This may be done by using two independent test objects on separate carriers, the examiner standing behind the patient and using a separate hand for each holder. Another method is to use a small black "paddle" type of carrier with two white test objects on it instead of one, and separated by  $1\frac{1}{2}$  or 2 inches (3.7 or 5 cm.),

so that there is one test object on each side of the vertical meridian as the carrier is brought centrally. I have described both these types of test object holders in a previous article.<sup>3</sup> The separate holders are probably better because they allow the examiner to vary the distance between the two test objects and thus come in radially as fixation is approached.

The patient may notice the test object on one side sooner than on the other, producing a level difference. In addition, once the two test objects are noticed, the patient may give helpful information that the object is definitely "clearer" or "more distinct" "or "brighter" on one side than on the other. This is substantially an indication of better quality of vision on that side and corresponds to the qualitative differences elicited by rapid comparisons. This method of simultaneous stimulation shows promise of becoming very useful in eliciting minimal defects, but I have not yet studied it fully enough to present any cases at present.

Actually, level differences elicited in this manner are comparable to the so-called attention defect except that the stimuli are much smaller, and therefore much smaller defects should be elicited.

#### SUMMARY

Three criteria are presented for detecting minimal field defects—level differences, rapid comparisons for qualitative differences and breadth of field. When only one of these criteria points to a defect, and to a defect of small extent, one must be extremely cautious about the interpretation. If two criteria are fulfilled and they point to the same type of field defect, one may be surer of their significance. The fulfilment of all three criteria is highly reliable as evidence of a defective field.

It goes without saying that roentgenography, air studies, electroencephalography and angiography must be used to corroborate the perimetrist's minimal field findings. However, the ophthalmologist must never forget that perimetry, no matter how well done, is still a subjective test, and he must temper his interpretations with a practical and clinical sense in committing himself to his neurologic and neurosurgical colleagues.

815 Park Avenue (21).

Dr. Margaret Rheinberger made the electroencephalographic studies used in this paper.

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3. Chamlin, M.: Technical Methods for the 1/2,000 Field, *Am. J. Ophth.* 30:1415 (Nov.) 1947.

# MECHANISM OF CORNEAL WOUND HEALING

## I. Cells Involved in Corneal Growth and Repair

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AND

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**I**N SPITE of the large amount of clinical and laboratory research work<sup>1</sup> that has been done, very little is actually known about the mechanism of corneal wound healing and the cells involved in this healing process. To this end we have aimed our research: first, to identify the cells involved and, second, to learn the mechanism of corneal wound healing.

### METHOD

A method has been worked out for maintaining rabbit corneal tissue in vitro apparently for an indefinite period. Fresh rabbit cornea is removed from the eye of the rabbit. The cornea is cut into pieces approximately 2 mm. square and 0.5 mm. thick. These pieces of tissue are planted in 3.5 D. Carrel flasks containing as a basic medium 0.7 cc. of Tyrode's solution, 0.3 cc. of rabbit serum, 0.5 cc. of chicken plasma and 1 drop of tissue extract of chick embryonic tissue (to facilitate formation of a coagulum). The cultures are kept in the incubator at a temperature of 38 C.

After twenty-four hours a supernatant layer of 0.5 cc. of rabbit serum is added to the cultures. The supernatant layer is removed after four days and the culture is washed with 0.1 cc. of Tyrode's solution for six hours, or even overnight. One-half cubic centimeter of fresh rabbit serum is then added. This procedure is repeated at four day intervals. After two weeks the cultures are divided and

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‡Lewis Cass Ledyard Jr. Fellow in Ophthalmology, with support in part from the Ettinger Fund.

The work of Mrs. Hoffman was supported in part by a grant from the Committee on Growth of the American Cancer Society.

1. Bajenova, M. A.: Culture of Preserved Corneal Tissue, *Arch. d'opht.* **53**:300, 1936. Castroviejo, R.: A Historical and Experimental Study of Keratoplasty, Including a New Method, *Am. J. Ophth.* **15**:825 and 905, 1932; Keratoplasty: Comments on Technic of Corneal Transplantation: Source and Preservation of Donor's Material; Report of New Instruments, *ibid.* **24**:1 and 139, 1941; Keratoplasty: Microscopic Study of the Corneal Grafts, *Tr. Am. Ophth. Soc.* **35**:355, 1937; Present Status of Keratoplasty, *Arch. Ophth.* **22**:114 (July) 1939. Filatov, V. P.: Transplantation of the Cornea from Preserved Cadaver's Eyes, *Lancet* **1**:1395, 1937. Elschmig, A., and Gradle, H. S.: History of Keratoplastic Operations to Date, *Am. J. Ophth.* **6**:998, 1923.

transplanted into fresh 3.5 D. Carrel flasks containing the same basic medium as that previously described and maintained in the same manner. Such cultures have been kept growing in our laboratory for fifteen months and are still in a healthy state. Addition of 0.5 cc. of an extract of adult sheep heart in Tyrode's solution possessing cell growth-promoting properties as a supernatant phase to the culture medium results in an area of growth approximately five times the size of that in cultures without cardiac extract.<sup>2</sup>

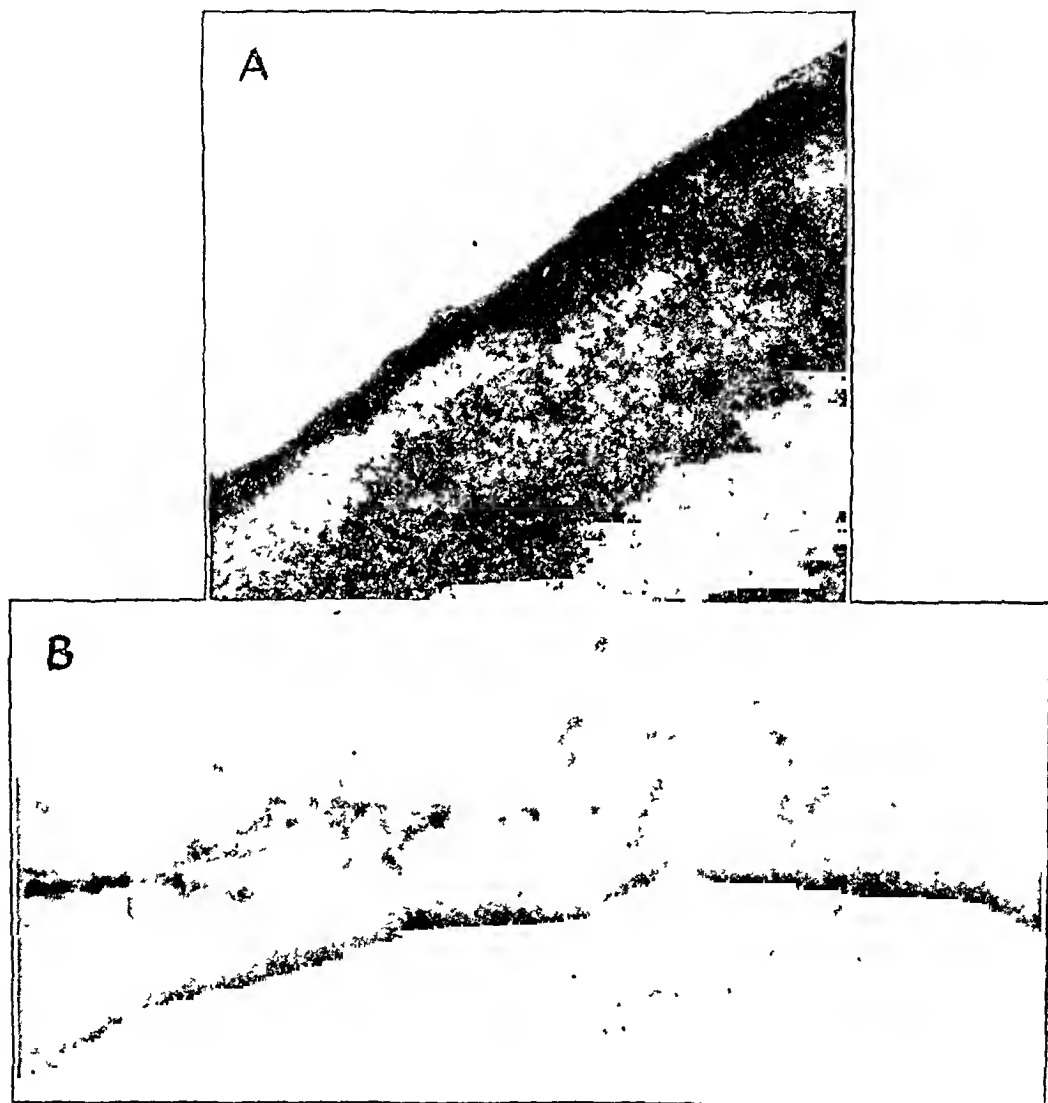


Fig. 1.—*A*, corneal tissue culture twenty hours after implantation. No cell division, proliferation or migration is present. *B*, corneal tissue culture twenty hours after implantation of cornea which had been irradiated with 30 r. Active cell division, proliferation and migration are present.

#### DESCRIPTION OF GROWTH

*Latent Period.*—When pieces of cornea are planted in vitro, as described, a period of from thirty to forty hours elapses before any

2. Hoffman, R. S., and Doljanski, L.: Growth Activating Effect of Extracts of Adult Tissue on Fibroblast Colonies in Vitro, *Growth* 3:61, 1939. Hoffman, R. S., and Wohlman, G. H.: Unpublished Data, 1948.

cells appear at the margin of the explant. This period is known as the latent period. The latent period may be considerably shortened by irradiating the freshly implanted cultures with small doses of roentgen radiation (30 r) (kilovolts; 25 mm. tungsten target; 0.5 mm. copper plus 1.65 mm. aluminum filter). After such irradiation the latent period is reduced to from fifteen to thirty hours (fig. 1 *A* and *B*). It may also be mentioned that, whereas normally only approximately 60 per cent of the fresh corneal implants grow in vitro, 98 per cent of the irradiated implants showed growth.

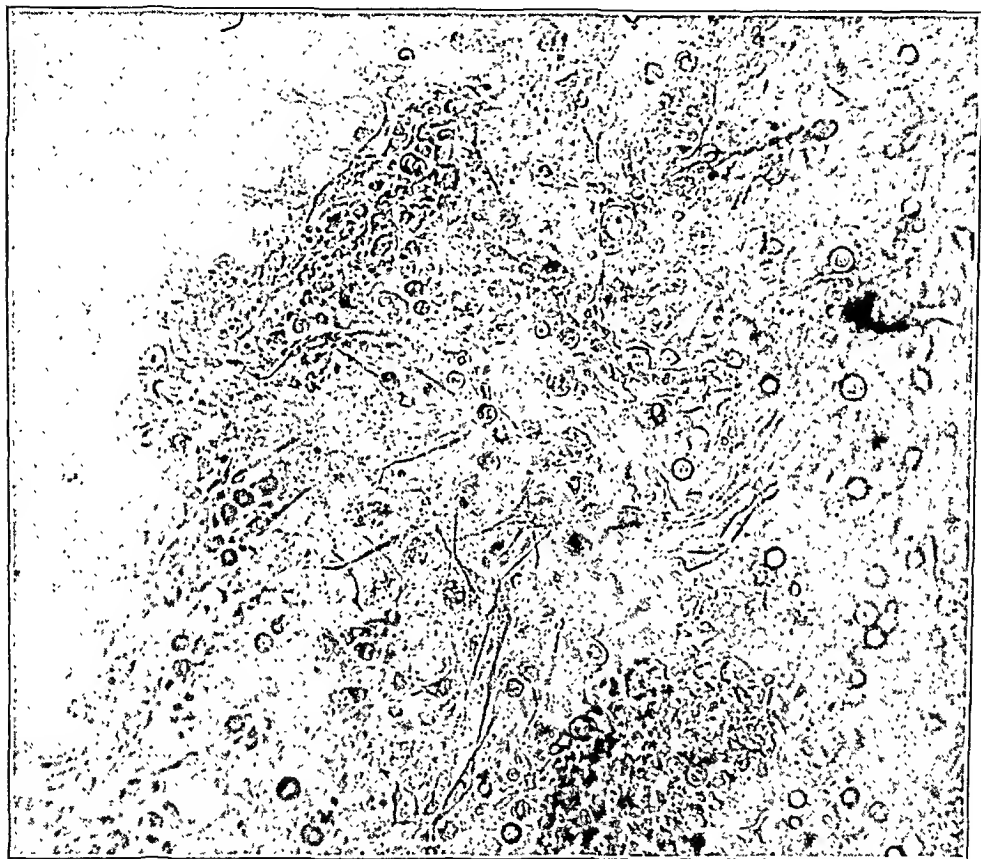


Fig. 2.—Corneal tissue culture fifty-four hours after implantation and treatment with growth-stimulating extract. Some epithelial cells are present, but the majority are corneal stroma cells, which vary in form from spindle to round cells.  $\times 100$ .

*Cell Types.*—The first cells to appear are a mixture of epithelial cells, round cells and long, spindle-shaped cells, which are presumably the stromal cells, or keratoblasts. The growth of the epithelial cells lasts only a short time, and then they die out. By merely scraping the epithelium from the cornea before putting it in the tissue culture, one can entirely eliminate the growth of epithelium. A number of intermediate stages are observed between the round cells and the stromal cells, and

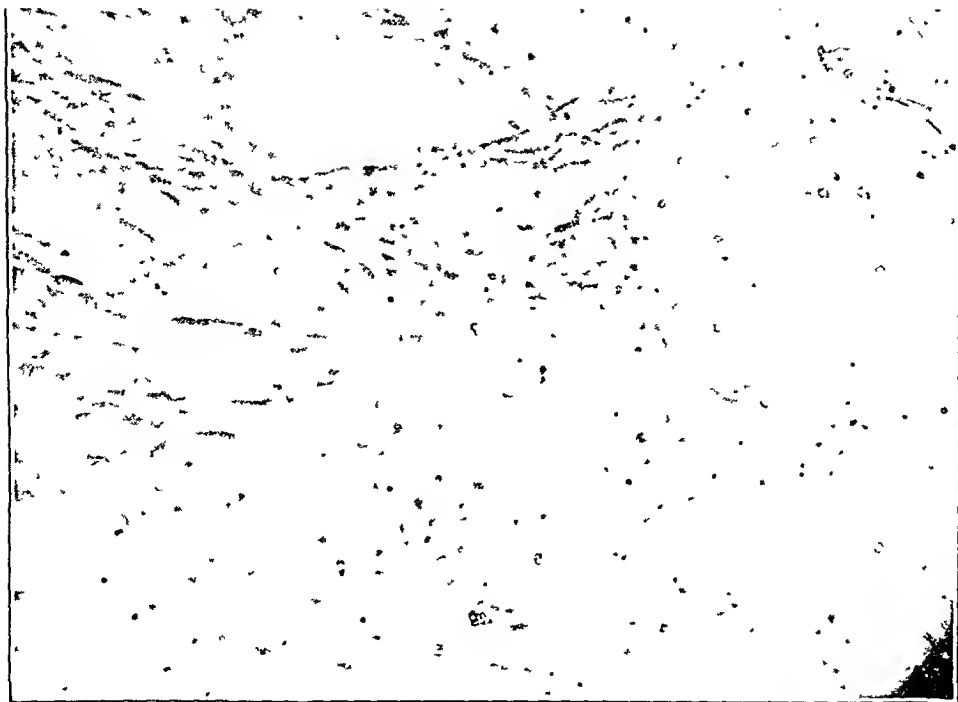


Fig. 3.—Corneal tissue culture eight months after the original implantation. The corneal stroma cells are now in the spindle cell form, and only a few round cell forms are present.  $\times 100$ .



Fig. 4.—*A*, rabbit cornea one day after freezing of the entire cornea and the adjacent sclera with carbon dioxide snow. There is diffuse edema of the entire cornea with engorgement of the anterior ciliary vessels.

*B*, rabbit cornea four days after freezing of the entire cornea and adjacent sclera with carbon dioxide snow. Clearing of the cornea has begun at the limbus on all sides, and this clearing is extending in toward the center of the cornea.

*C*, rabbit cornea fourteen days after freezing of the entire cornea and adjacent sclera with carbon dioxide snow. The cornea has now completely regained its transparency, but corneal sensation does not return for four to six months.

this interchangeability can also be observed in response to changes in the temperature surrounding the tissue culture. Under normal conditions these cells have long, tapering spindle processes and a small, elongated nucleus and resemble fibrocytes very closely; but in response to environmental changes these cells appear to retract their processes and assume a round form, much like that of a large macrophage. This interchangeability in form of the cells lasts for about two weeks; then



Fig. 5.—Cornea of eye enucleated four days after freezing of the entire cornea. No viable cells are present; only pyknotic and fragmented nuclear material are to be seen. Hematoxylin-eosin stain;  $\times 450$ .

the fibrocytes take on the appearance of an almost pure strain of fibrocytes, with only a few round cells present (figs. 2 and 3).

#### CARBON DIOXIDE SNOW-FREEZING EXPERIMENTS

A brass container with a bottom 5 mm. square and 0.5 mm thick was devised to hold carbon dioxide snow for experiments in freezing the

cornea in the living animal. A portion of the cornea was frozen for one minute and then allowed to thaw out.

When the entire cornea and a portion of the adjacent sclera was frozen for one minute, forty-five seconds was required for the cornea to thaw out. Moderately severe edema involving all layers of the cornea developed within one hour (fig. 4 *A*). This edema persisted until the fourth day (fig. 4 *B*), when clearing was observed around the periphery of the cornea; and this clearing gradually widened toward the center of the cornea, until by the fifteenth day (fig. 4 *C*) the entire cornea was once again clear. For control purposes, portions of cornea

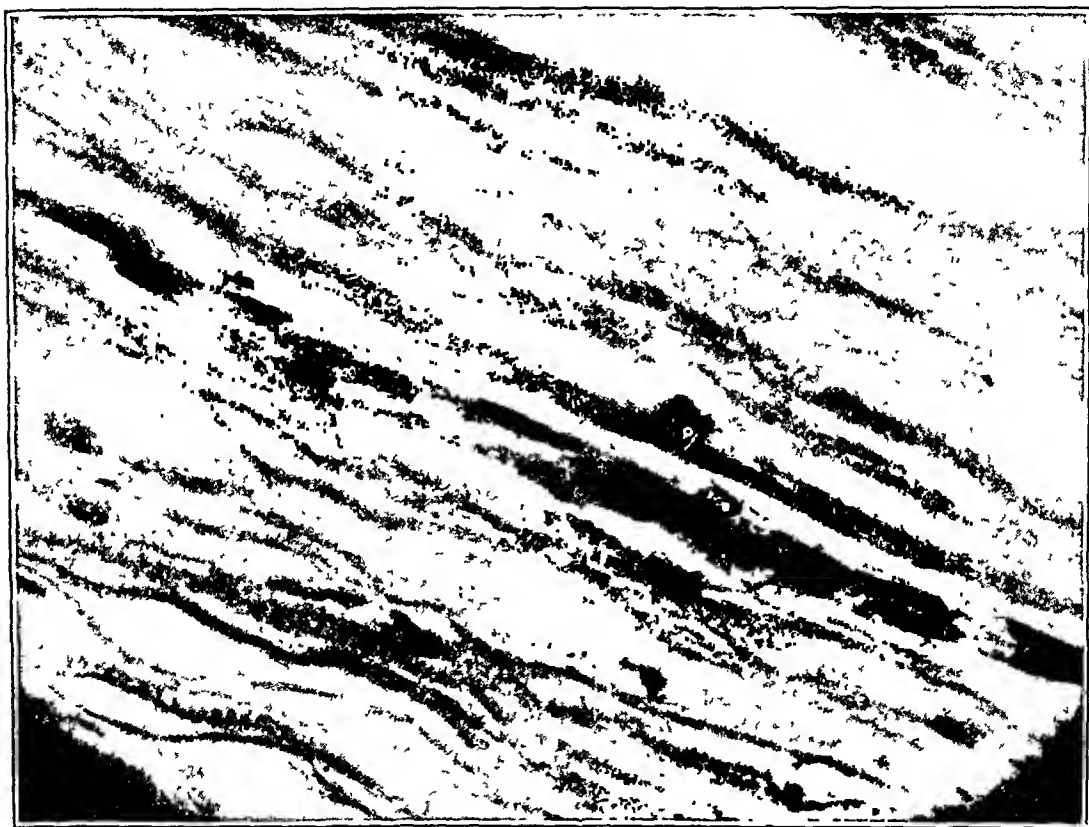


Fig. 6.—Cornea removed ten days after freezing of the entire cornea. Fibrocytes are entering the devitalized cornea from the limbus and are proceeding along lamellar interspaces. A few fragmented nuclei and empty cell spaces are still seen. Hematoxylin-eosin stain;  $\times 450$ .

were removed immediately after freezing, and these portions of cornea were placed in tissue cultures, where no growth was observed at any time (fig. 5).

We assumed that the returning transparency of the frozen cornea was brought about by fibrocytes migrating from the surrounding fibrous structures into the devitalized cornea. After migrating into the devitalized cornea, these cells assumed the characteristics and functions of stromal cells. The areas of clearing paralleled the progress of the cells migrating into the devitalized cornea, and the areas which were not



invaded remained edematous and cloudy until the migrating cells reached this area. Sections of eyes removed at various times after freezing of the cornea showed these cells entering the periphery of the cornea, and the center of the cornea had no viable cells until the fifteenth day, when clearing was complete (fig. 6 and 7).

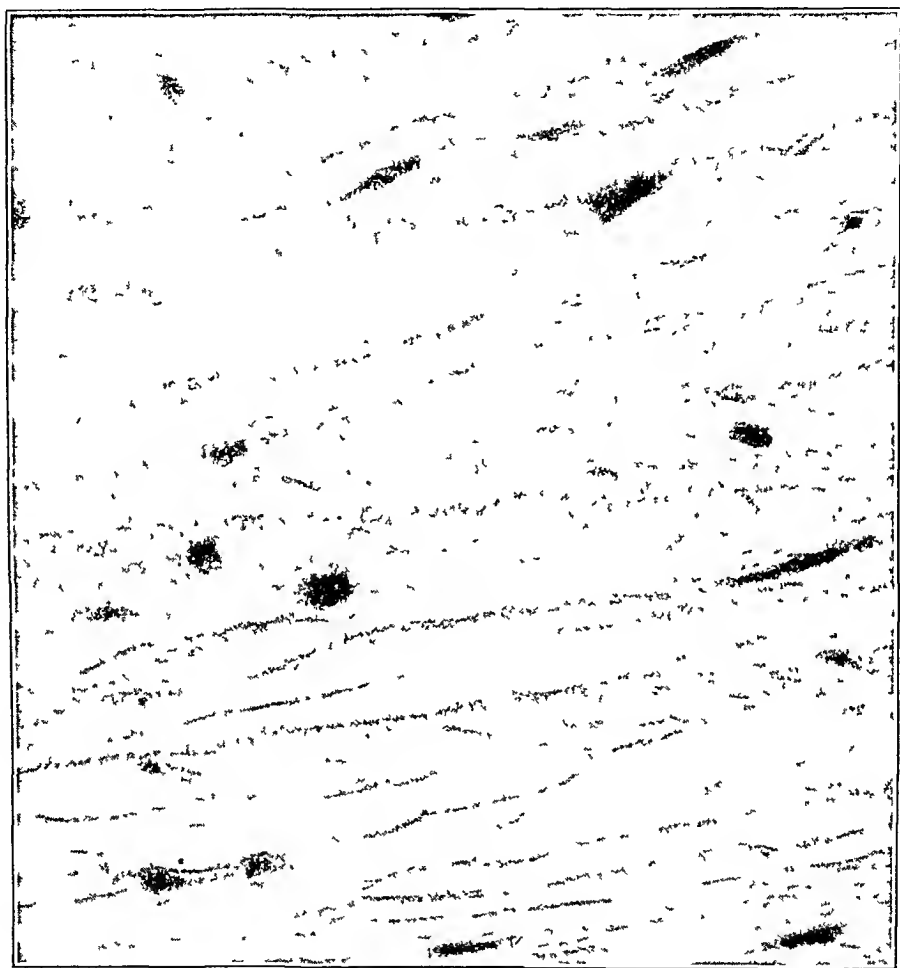


Fig. 7—Cornea removed fourteen days after freezing of the entire cornea. The previously devitalized cornea has been completely repopulated by fibrocytes migrating from surrounding fibrous structures. With these invading cells also returns the transparency of the cornea. Hematoxylin-eosin stain;  $\times 450$ .

#### SUMMARY AND CONCLUSIONS

A method was worked out for preserving rabbit corneal tissue *in vitro* indefinitely.

A pattern of growth of corneal stromal cells was observed. This pattern includes a definite latent period before any growth is observed and a noticeable interchangeability in form of the stromal cells in response to changes in environment.

The latent period of growth in the tissue cultures can be appreciably shortened by low dosage irradiation, and the amount of growth can be increased by the addition of aqueous sheep heart extract possessing stimulating properties to the tissue culture mediums.

The cells obtained on culture of corneal tissue exhibit the characteristics of fibrocytes.

The corneal stroma cells are not specific for the cornea but may be derived by migration from adjacent fibrous tissues. On entering the cornea, these cells, from adjacent fibrous structures, conform to the lamellar arrangement and assume the characteristics and functions of stroma cells.

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# MECHANISM OF CORNEAL GRAFT HEALING

## II. Behavior of Recipient and Donor Cells

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THE PURPOSE of this paper is to clarify the long-debated problem of the true nature of a corneal graft. The crux of the problem is whether a corneal graft heals like a skin graft, in other words like a "true" graft, or like a boiled bone or preserved cartilage graft, often called a "replacement" graft.

The previous work on cultures of corneal tissue has shown that the cells of the corneal stroma have the ability to divide and migrate.<sup>1</sup> With this in mind, it was felt that if a corneal graft were a "true" graft then donor cornea the cells of which had been "activated" by growth in tissue culture should heal rapidly in the recipient cornea. Accordingly, pieces of donor cornea were grown in tissue culture for varying lengths of time and then transplanted into the recipient corneas. Instead of rapid healing, all eyes revealed a marked repellent reaction on the part of the recipient cornea to all attempts of the donor cells to grow into the recipient cornea (figs. 1 and 2). The reaction was inflammatory in nature and was evidenced by numerous polymorphonuclear leukocytes, macrophages, fibrocytes and neovascularization of the recipient cornea. This inflammation persisted until the donor cells had died and healing had started from the deeper layers of the cornea; as healing progressed, it appeared to push out or extrude the necrotic remains of the donor material, and the end result was a dense fibrous replacement scar of the cornea.

The next step was to repeat work already reported by other investigators on the transplantation of frozen donor cornea.<sup>2</sup> From the freezing experiments previously mentioned,<sup>1</sup> it was known that a frozen piece of cornea was a devitalized tissue in that no visible cells were left after freezing. It was assumed that if a frozen donor cornea should

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The work of Mrs. Hoffman was supported in part by a grant from the American Cancer Society.

1. Hoffman, R. S., and Messier, P. E.: Mechanism of Corneal Wound Healing: I. Cells Involved in Corneal Growth and Repair, *Arch Ophth.* **42**:140 (Aug.) 1949.

2. Weiss, P., and Taylor, A. C.: Transplantation of Frozen Dried Corneas in the Rat, *Anat. Rec.* **82**:49, 1944.

heal normally and remain transparent the healing and maintenance of transparency must have been the function of the cells of the recipient cornea. Accordingly, corneal grafts were made with the donor cornea frozen for periods varying from twenty-four hours to four months before transplantation. All these grafts exhibited the same pattern, which consisted of healing of the wound edges and maintenance of



Fig. 1.—Section of cultured donor cornea and recipient cornea six days after transplantation. There is no union of edges, and fibrous growth from the deeper part of the recipient cornea is undermining the donor cornea. In the nonunion areas are accumulations of leukocytes, which form a constant part of this reaction. Hematoxylin-eosin stain;  $\times 100$ .

transparency, the latter lasting until the tenth to the twelfth day. At this time the center of the graft became cloudy and edematous, and this area either remained opaque or became necrotic and sloughed out, the resultant picture being a dense fibrous replacement scar.

## FREEZING EXPERIMENTS

With the carbon dioxide applicator previously described, a 5 mm. square in the center of the living cornea was frozen for one minute. This area thawed out within thirty seconds. Minimal edema of the superficial layers of the area developed and lasted for about forty-eight hours, at which time transparency and complete healing of the area had been effected by the cells migrating from the intact portion of the cornea into the devitalized area.

However, when these frozen areas in the cornea were surrounded by cuts of varying depth, different results were obtained. When the surrounding cuts were shallow, there developed in the enclosed area a mod-

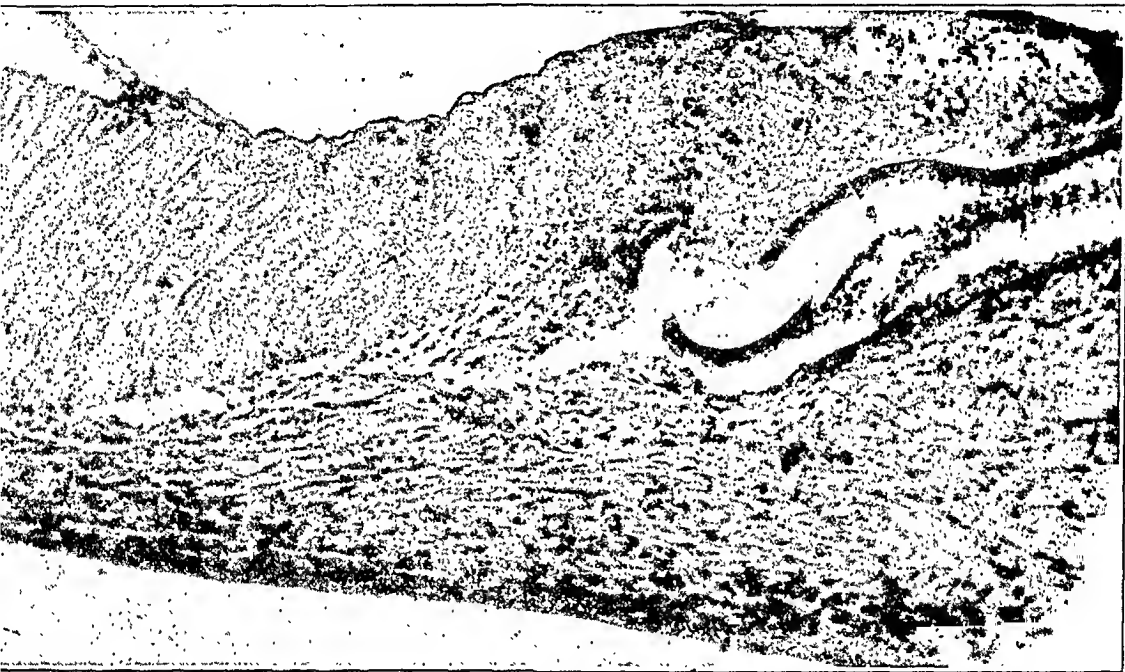


Fig. 2.—Section of cultured donor cornea and recipient cornea fourteen days after transplantation. There is still no union between the two pieces of tissue, and the growth from the deeper part of the recipient cornea has completely undermined the donor cornea, this process continuing until the donor cornea is extruded entirely from the recipient cornea. Hematoxylin-eosin stain;  $\times 100$ .

erate amount of edema, which lasted three days and then cleared, with complete healing of the cuts at the end of five days (fig. 3 *A* and *B*). When the cuts were deep, the result was the same as with the frozen donor material; i. e., the area became cloudy and either remained opaque or became necrotic and sloughed out (fig. 3 *C* and *D*). When the cuts were deep but did not completely join each other, moderate edema of the frozen area developed, but clearing began at the point where the cuts were incomplete and from this point spread to involve the whole area.

Microscopic examination of these eyes showed that when the cuts in the cornea were deep the frozen cornea beneath the level of the cuts was rapidly repopulated by cells migrating from the surrounding, normal, cornea. However, the frozen area above the level of the corneal cuts received none of these migrating cells because the course of these cells was restricted to the plane of the lamellar structure in which they entered. Instead, the frozen area above the level of the cuts

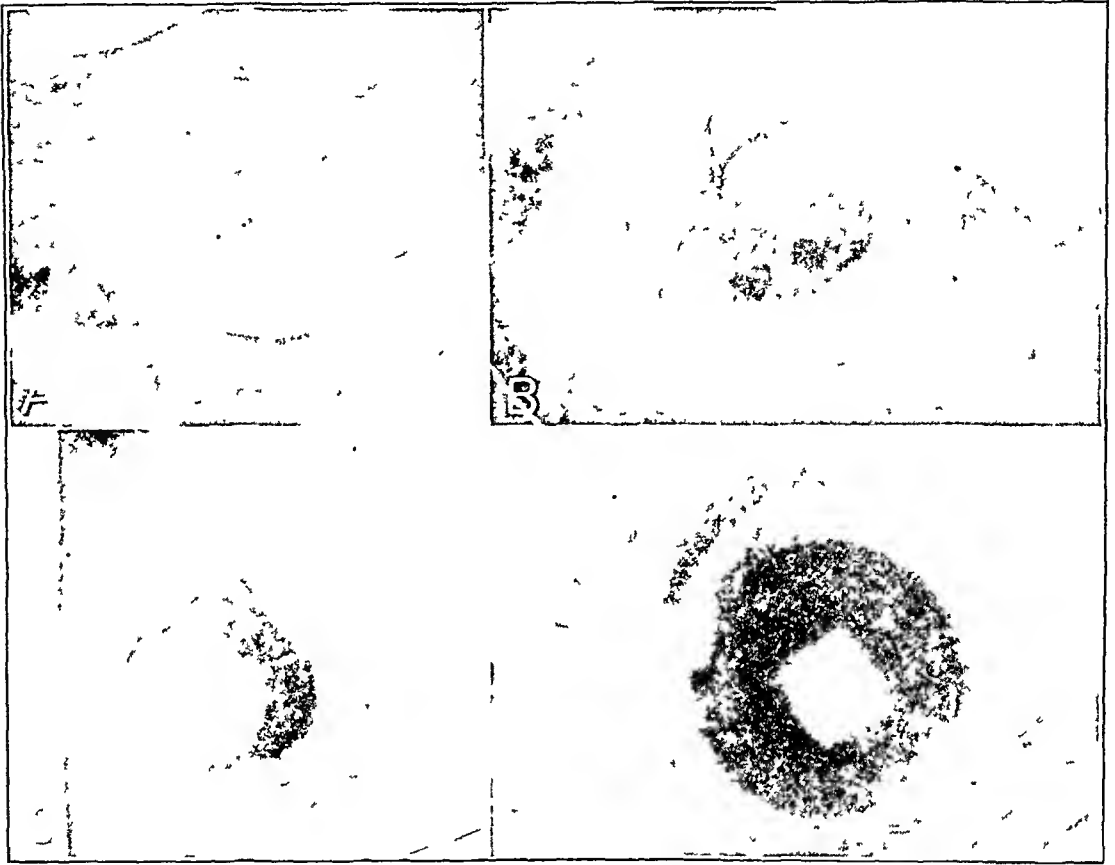


Fig. 3.—*A*, rabbit cornea three days after freezing of a 5 mm. square surrounded by connecting shallow cuts in the cornea. Within the area outlined by the shallow cuts the cornea is moderately edematous and hazy.

*B*, rabbit cornea five days after freezing of a 5 mm. square surrounded by connecting shallow cuts in the cornea. The cells from the normal cornea have now passed the barrier of shallow cuts and have entered the devitalized area; parallel with the entrance of these cells is the return of transparency to the area. The cuts in the cornea are healed by the invading cells, which are arranged in typical scar fashion.

*C*, rabbit cornea eight days after freezing of a 5 mm. square surrounded by connecting deep cuts in the cornea. Within the area outlined by the deep cuts the cornea is highly edematous and hazy and the edges are beginning to slough. The cells from the normal cornea have been prevented by the deep cuts in the cornea from entering the frozen area, and this devitalized cornea is now undergoing necrosis.

*D*, rabbit cornea twenty-one days after freezing of a 5 mm. square surrounded by connecting deep cuts in the cornea. The devitalized and necrotic portion of the cornea outlined by the deep cuts has finally been entered by the cells from the normal cornea, but, because this area has undergone necrosis, there is no normal lamellar arrangement to guide these entering cells, and the cells arrange themselves in typical scar formation.

showed only pyknotic nuclear fragments, marked edema and, finally, necrosis and destruction of the lamellar structure (fig. 4). With the destruction of the lamellar structure, cells migrated into the area and arranged themselves in the typical whorling fashion of scar tissue.

Since the healing and maintenance of transparency of the frozen area or frozen graft appeared to be dependent on the rapid passage of the recipient cells across the wound edges, frozen donor material was again grafted into recipient corneas and, after operation, treated vigor-

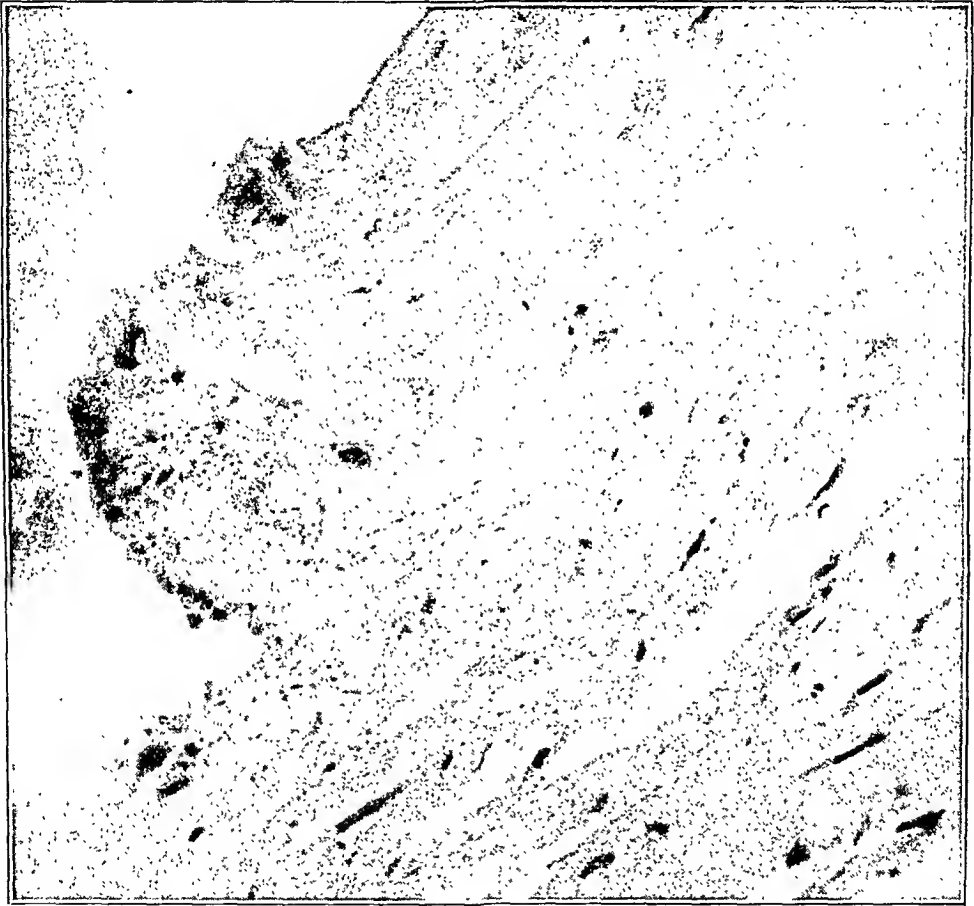


Fig. 4.—Section of a rabbit cornea four days after freezing of a 5 mm. square surrounded by connecting deep cuts in the cornea. That portion of the frozen area which is beneath the level of the cut in the cornea is now repopulated with cells migrating from the normal cornea. The portion of the frozen area which is above the level of the deep cut in the cornea has only pyknotic nuclear fragments, is edematous and shows beginning disintegration of the lamellar structure. With the loss of the lamellar structure in this area, the migrating cells enter and form a typical scar, as shown in figure 3 *D*.

ously with growth extract. However, this procedure appeared to have little effect on the final result, which was necrosis and scarring of the graft.

## COMMENT

The results with the tissue culture-grown donor material appear to represent a definite repellent reaction on the part of the recipient cornea to any attempts of the donor cells to grow into the recipient cornea or to have any part in the healing of the wound edges. It is not until all the donor cells have died that any attempts at healing are made, and these appear to be made by the recipient cells; and, in addition to healing, this process appears to expel the dead donor tissue as healing progresses. From this experiment, it would appear that the donor cells have no part in the healing of a corneal graft.

The carbon dioxide-freezing experiments reveal that corneal stroma cells can migrate into a devitalized area and carry on the normal function of stromal cells in this area. However, if the frozen areas are surrounded by deep cuts, or even completely penetrating cuts, as in the case of the frozen grafts, the result is either complete scarring of the area or necrosis and sloughing of the area. It appears that the reason for this failure of the frozen areas to become transparent again was that the cells were unable to cross the wound edges fast enough to take up the normal metabolism of the area, which had been devitalized by the freezing process. The experiments with the deep cuts which did not completely surround the frozen area showed that the frozen area can again become transparent, provided that the cells from the normal cornea can enter the devitalized area quickly to take up the metabolism of this area, even though the path of entrance is limited to a very small bridge of corneal tissue.

## SUMMARY

1. Corneal grafts made with donor material grown in tissue culture before operation caused a marked repellent reaction on the part of the recipient cornea to all attempts of the donor cells to grow into the recipient cornea.

2. Corneal grafts performed with donor material frozen before operation resulted in healing of the edges but with necrosis and scarring of the center of the graft.

3. Freezing experiments showed that stromal cells from the normal cornea can migrate into a devitalized area and take up the normal metabolism of this area, provided that entrance of these cells into the area is not delayed too long in passage across the wound edges.

4. The application of growth extract after operation to grafts made with frozen donor material did not sufficiently hasten the passage of the recipient fibrocytes across the wound edges, and necrosis and scarring resulted before healing had been accomplished.



## CONCLUSIONS

It would appear that the cells in the donor cornea have no part in the healing of a corneal graft; rather, healing is the function of the cells of the recipient cornea. The maintenance of transparency of the graft appears to depend on the rapid passage of the recipient cells into the donor tissue when devitalized donor material is used. With the use of donor material at present limited to fresh material, it appears that the viable cells in the fresh donor material are capable of carrying on metabolism in the donor tissue until they are replaced by the cells of the recipient cornea. On the basis of the foregoing information, it is felt that a corneal graft should be classified as a replacement type graft.

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## CIRCULAR CORNEAL TRANSPLANTS

Surgical Technic; Instruments and Sutures; Comparison with the Use of Square Transplants

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**M**OST OF the early investigators of corneal transplantation used circular corneal grafts. Von Hippel<sup>1</sup> introduced a corneal trephine and fathered a style of keratoplasty. Elschmig<sup>2</sup> and Filatov<sup>3</sup> adopted von Hippel's general technic and added modifications of their own invention. Thomas,<sup>4</sup> who introduced corneal transplantation to England, used square corneal grafts in his early experiments on rabbits, but later abandoned this procedure in favor of the circular type. Thomas described a tendency of the corners of the square graft to protrude, and even become detached; he also found that one of the loops of the suture frequently came to lie in the incision, thus preventing proper union of the wound. Castroviejo likewise introduced corneal transplantation to the United States. Working at the Mayo Clinic in 1931, he<sup>5</sup> initially performed corneal transplantations on rabbits, following the technics of Elschmig and Thomas; but these operations were all failures. Then Castroviejo<sup>6</sup> devised his own technic, employing first rectangular and later square grafts, with a gratifying percentage of successful operations on laboratory animals. Since that time, he has reported<sup>7</sup> many success-

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1. von Hippel, A.: Eine neue Methode der Hornhauttransplantation, Arch. f. Ophth. **34**:108-130, 1888.

2. Elschmig, A.: Keratoplasty, Arch. Ophth. **4**:165-173 (Aug.) 1930.

3. Filatov, V. P.: Transplantation of the Cornea, Arch. Ophth. **13**:321-347 (March) 1935.

4. Thomas, J. W. T.: Transplantation of the Cornea: A Preliminary Report on a Series of Experiments on Rabbits, Together with a Demonstration of Four Rabbits with Clear Corneal Grafts, Tr. Ophth. Soc. U. Kingdom **50**:127-141, 1930; Successful Grafting of the Cornea in Rabbits, Lancet **1**:335-341, 1931.

5. Castroviejo, R.: Preliminary Report of a New Method of Corneal Transplant, Proc. Staff Meet., Mayo Clin. **6**:417-418, 1931.

6. Castroviejo, R.: New Method of Corneal Transplantation: Final Report, Proc. Staff Meet., Mayo Clin. **6**:669, 1931; Keratoplasty: An Historical and Experimental Study, Including a New Method, Am. J. Ophth. **15**:825-838 and 905-916, 1932.

7. Castroviejo, R.: (a) Keratoplasty: III. Report of Seven Cases, Am. J. Ophth. **17**:932-945, 1934; (b) Queratoplastia: estudio clínico de catorce casos; la córnea de feto como material de transplante, Arch. de oftal. hispano-am. **35**:404-434, 1935; (c) Keratoplasty: Report of Cases, with Special Reference to Compli-

ful operations on patients and has remained a staunch advocate of the use of square corneal transplants.

Studying at the same institution where Castroviejo conducted much of his research and performed many corneal transplantations, it was natural that I should first employ the square type of corneal graft. The surgical technic of this procedure was discussed in a previous communication<sup>8</sup> (with Dr. J. A. C. Wadsworth). However, regardless of the number of operations performed, transplantation of the square corneal graft remained a difficult procedure, with uncertain results. Strangely, the greatest difficulty with this type of keratoplasty was found in obtaining a square graft and a square window to receive it. It is not simple to apply two straight-cutting blades to a curved surface like the cornea and make two identical, superficial incisions at the same time. It is even more difficult to make the second pair of lines at exact right angles to the first; if this is not done, the resulting figure is not square. After the green mark is made and the anterior chamber incised with the keratome, completion of the incision with scissors is not easy, and cutting the square corners is particularly intricate. When the operation is finished, the corners of the graft exhibit a decided tendency to bulge forward unless the suture passes exactly over the apex of each corner. Because of these difficulties, circular corneal transplants have been tried and now appear to possess certain definite advantages over the square type. The purpose of this paper is to describe the technic of transplantation of circular corneal grafts and to compare this operation with that using the square graft.

#### TECHNIC OF TRANSPLANTATION

*Equipment Required for the Operation.*—The instruments employed in securing the circular type of corneal transplant are less complicated than those used in the square type. A corneal trephine and a pair of curved corneal scissors take the place of the double-bladed knife, the special keratome and the straight corneal scissors. The following instruments are recommended (fig. 1): (1) Elschnig's fixation forceps, for immobilizing the eye; (2) a 4.5, 5.5 or 6.5 mm. corneal trephine, for marking out the window in the recipient eye and for making the

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cated Ones, J. M. Soc. New Jersey **32**:80-88, 1935; (d) Surgery of the Cornea, Internat. Abstr. Surg. **65**:489-505, 1937; (e) Results of Corneal Transplantation, Arch. Ophth. **19**:834-835 (May) 1938; (f) Present Status of Keratoplasty, *ibid.* **22**:114-126 (July) 1939; (g) Keratoplasty: Comments on the Technique of Corneal Transplantation: Source and Preservation of Donor's Material; Report of New Instruments, Am. J. Ophth. **24**:1-20 and 139-155, 1941; (h) Indications and Contra-Indications for Keratoplasty and Keratectomies, Tr. Am. Ophth. Soc. **43**:324-330, 1945; Am. J. Ophth. **29**:1081-1089, 1946; (i) Corneal Transplantation, Am. J. Nursing **46**:31-34, 1946.

8. Stansbury, F. C., and Wadsworth, J. A. C.: Surgical Technique of Corneal Transplantation in Rabbits: A Discussion of the Problems Encountered and Suggestions for Their Solution, Am. J. Ophth. **30**:968-978, 1947.

incision into the anterior chamber in both eyes; (3) a fine needle holder, for placing the sutures; (4) curved, modified de Wecker corneal scissors, for completion of the incision into the anterior chamber; (5) spatula, for transferring the graft from the donor eye to the recipient eye and making small adjustments in the position of the graft; (6) small, straight toothless forceps, and (7) small, curved, toothless forceps, for tying the sutures; (8) a standard eye speculum; (9) suture

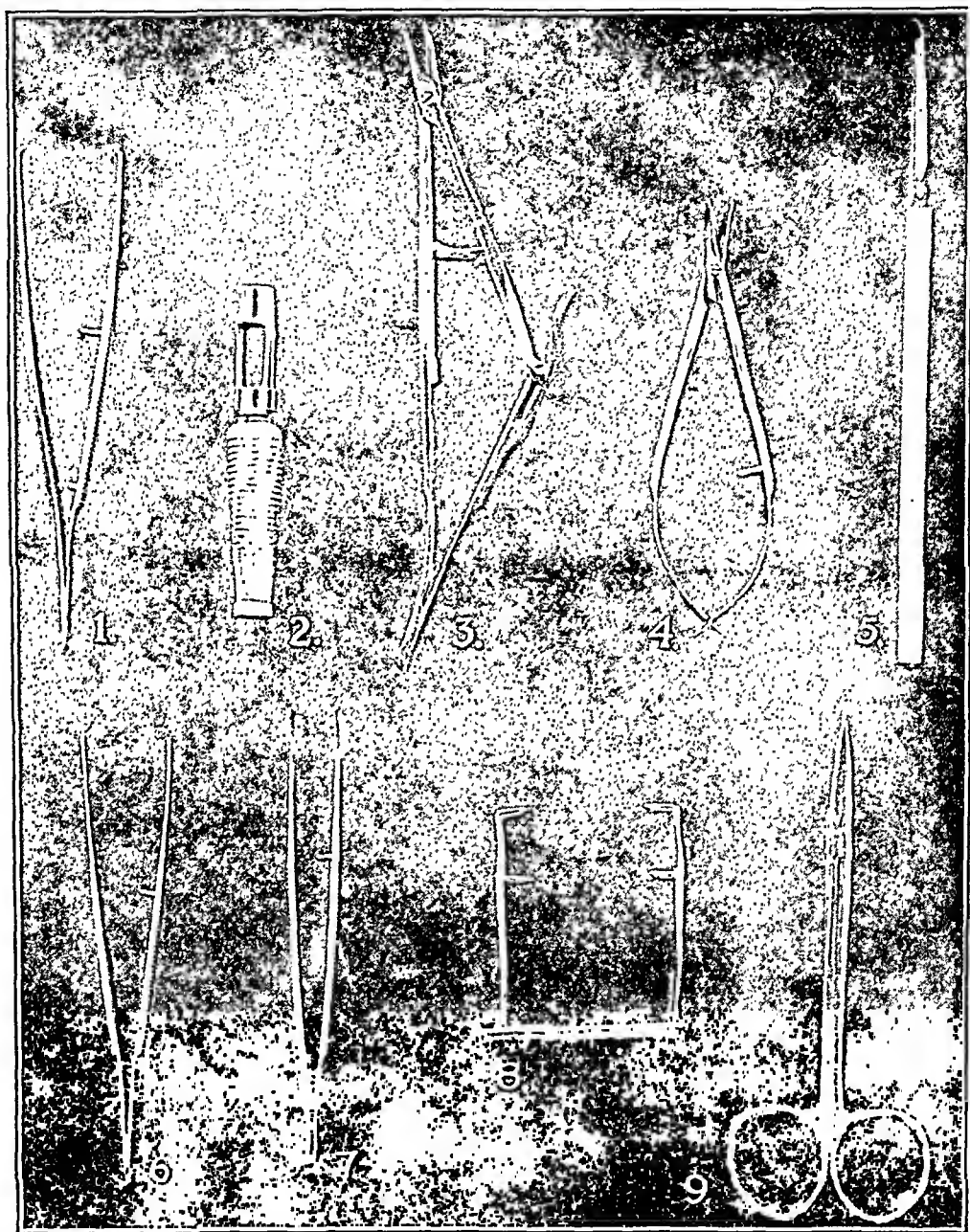


Fig. 1.—Recommended instruments: 1, Elschnig's fixation forceps; 2, Elliott type of corneal trephine; 3, needle holder; 4, curved, modified de Wecker scissors; 5, spatula; 6, small, straight toothless forceps; 7, small, curved toothless forceps; 8, speculum, and 9, suture scissors.

scissors, and (10) two 000000 single-armed, black silk corneal sutures, with atraumatic needles.<sup>®</sup>

The following preparations are used during the operation: (1) 3.5 per cent iodine solution, and (2) 70 per cent alcohol, for preparing the skin about the

operative field; (3) 4 per cent cocaine solution, for use as drops in the conjunctival sac and for subconjunctival injection; (4) 2 per cent procaine solution, for local anesthesia about the eye, to be injected subcutaneously, and for the retrobulbar injection; (5) 25 per cent solution of mild protein silver, and (6) 1:1000 aqueous solution of epinephrine hydrochloride, for flushing out the conjunctival sac; (7) 2 per cent solution of fluorescein sodium, for staining the superficial corneal incision in the host eye; (8) Ringer's solution, for irrigation; (9) 3 per cent atropine solution, and (10) 1 per cent atropine ointment, to be instilled in the conjunctival sac at the close of the operation.

*Preoperative Procedure.*—The patient should be admitted to the hospital on the day before corneal transplantation is anticipated. Cultures of material from the conjunctival sac are taken the night before operation. Kodachrome® photographs of the eye are obtained. A final examination of the eye with the slit lamp is worth while to the surgeon. The condition of the recipient cornea, such as thickness or thinness, edema, vascularization, location and depth of scars and presence or absence of anterior synechias should be carefully ascertained. In a case of keratoconus, the location of the apex of the conus and the condition of the surrounding cornea are particularly important. The size and location of the transplant should be decided at the examination with the slit lamp. The reactivity of the pupil and the presence or absence of posterior synechias are noted. The general behavior of the patient is studied; an apprehensive patient is a poor subject for corneal transplantation, particularly when local anesthesia is used. If the patient falls into this category, or if the patient is a child, general anesthesia is indicated.

A cathartic is administered the night before operation, and a soapsuds enema is given the next morning. If the operation is to be in the afternoon, a fluid lunch is prescribed; if in the morning, breakfast is omitted. Two hours before operation, 0.2 Gm. of pentobarbital sodium U. S. P. is given and, one hour before operation, another 0.1 Gm. of the same drug is administered. The pupil of the eye to be operated in is dilated with 10 per cent phenylephrine hydrochloride (neo-synephrine hydrochloride®) and 5 per cent hemotropine hydrobromide, 1 drop of each drug every fifteen minutes, beginning two hours before operation, and kept dilated with these drugs until the patient goes to the operating room.

*Surgical Procedure.*—The skin about the eye to be operated on is scrubbed with 3.5 per cent solution of iodine, and then with 70 per cent alcohol. A 4 per cent solution of cocaine is instilled into the conjunctival sac. The operative field is draped with sterile towels. Local anesthesia, employing 2 per cent solution of procaine, is given by subcutaneous injection into the periorbital region. A retrobulbar injection of 1.5 cc. of 2 per cent procaine solution is given, and a small amount of 4 per cent cocaine solution is injected subconjunctivally, in the upper and lower fornices. The conjunctival sac is filled with 25 per cent solution of mild protein silver U. S. P. and washed out with 1:1,000 solution of epinephrine hydrochloride. A speculum is inserted between the lids.

The eye is fixated with Elschnig's fixation forceps, and the corneal circle to be removed is marked out by a superficial incision with the corneal trephine. A drop of 2 per cent solution of fluorescein sodium is dropped on this circle and quickly washed away with Ringer's solution. Using 000000 or 0000000 single-armed, black silk corneal sutures, with atraumatic needles,® one now places two sutures in the corneal stroma about the green circle (figs. 2 and 4). With the first suture, a bite is made in the cornea from 10 to 8 o'clock, so that the buried portion of the suture is about 1 mm. from the fluorescein-stained circle. The same needle is then reintroduced at 2 o'clock and brought out at 4 o'clock. The two ends of

this suture are laid to either side, and the loop from 8 to 2 o'clock is placed either above or below the window to be excised. With the other suture, a bite is made from 1 to 11 o'clock, and another, from 5 to 7 o'clock. The ends of this suture are likewise extended above and below the cornea, respectively, and the loop formed placed to either side of the window to be excised. In placing these corneal sutures, care is taken to insure that the intracorneal portions (at 12, 3, 6 and 9 o'clock) are at least 1 mm., and preferably not more than 1.5 mm., from the green circle. It is essential to place these intracorneal bites symmetrically about the circle, so that all four segments within the corneal stroma are of the same length and so that the opposing intracorneal segments are parallel and directly opposite each other. If this is done, the suture when tied will divide the corneal circle into eight equal parts (like the pieces of a pie). One of the suture ends with a needle is then severed, and a Moss suture is placed in the corneal stroma in the center of the circle; this is loosely tied and the ends are cut 1 or 2 mm. from the knot.

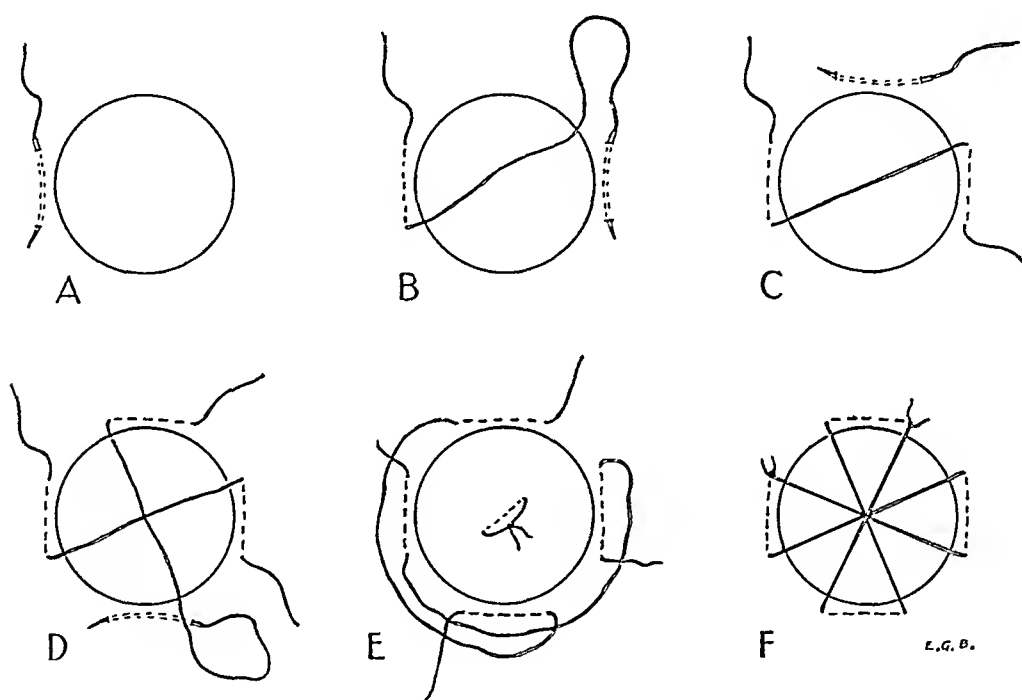


Fig. 2.—Diagram illustrating the steps in placing the two sutures in the cornea. *A* and *B* show the insertion of the first suture, and *C* and *D*, the insertion of the second suture. *E* shows the loops removed from the incision and the Moss suture; *F*, the completed suture pattern.

The donor eye is then held in a piece of gauze bandage, and a trephine incision is made through the center of the cornea into the anterior chamber. An attempt is made to hold the trephine "normal" to the cornea, in order that the incision into the anterior chamber may be as large as possible. Seldom, however, is the resulting incision through Descemet's membrane larger than one-third the circumference of the circle. One completes the remainder of this incision with the curved corneal scissors, avoiding any manipulation of the round disk which is being excised. No attempt is made to cut the incision on a bevel, either in the donor eye or in the host's cornea. Careful observation of the incision will disclose that the circle on the endothelial side of the cornea is always slightly smaller than the one on the epithelial aspect, without any conscious attempt to make a bevel. The graft is removed from the donor eye with a spatula and placed in a beaker of Ringer's

solution; it is washed about in this solution to remove any fragments of iris pigment clinging to its posterior surface.

The recipient eye is again fixated with Elschnig forceps, and the position of the sutures is checked, to make sure that they are free from the incision. The corneal trephine is then reapplied to the green circle in the epithelium, and the incision is carried down into the anterior chamber. As soon as the iris is seen to move, the trephine is removed. The portion of cornea to be excised is lifted slightly above the lens by traction on the Moss suture, and incision of the rest of the circle is completed with the fine, curved corneal scissors. The curvature of the circle is most accurately followed by employing a number of short bites with the scissors, rather than a few long ones. After the incision is completed and the window formed, the donor graft is removed from the Ringer solution with the spatula and placed in the window in the recipient cornea. The excised corneal disk from the host's eye is sent to the pathologic laboratory for examination. The sutures are then tied with the pair of small toothless forceps. One of the loops is picked up in the curve of the curved forceps, and either end of this suture is pulled with the other forceps until the loop lies in its proper place across the graft. The remaining loop is then picked up and drawn into position in the same manner. If the horizontal suture is to be tied first, the two ends are brought together, either at 10 or 4 o'clock, depending on the convenience of either site, and tied. Likewise, the vertical suture may be tied either at 1 or at 7 o'clock. Either one of the sutures may be tightened first, and either one may be tied first. Care is exercised to tie the sutures as close to the bite in the cornea as possible, so that the knot will not lie over the incision. The tied sutures should not be taut over the graft.

The position of the graft is then adjusted with the spatula, as good an approximation of the wound edges as possible being secured. Air may be injected into the anterior chamber at this time, in the same manner as after cataract extraction. Ordinarily, this is not necessary, as the anterior chamber will begin to reform before the end of the operation; it is a useful maneuver, however, when there is any particular reason to fear anterior synechias. A 3 per cent solution of atropine is instilled into the conjunctival sac. The speculum is removed and an ointment containing 1 per cent atropine sulfate instilled into the conjunctival sac. The lids are closed, and a binocular bandage is applied. A fiber mask is tied around the patient's head for protection, and he is taken back to his bed.

*Postoperative Care.*—Absolute bed rest is prescribed for the first nine days. Codeine and acetylsalicylic acid are given for relief of pain in the eye. One of the barbiturates is usually given two or three times a day during this period; every attempt is made to keep the patient as quiet as possible. A light diet is given, and bowel movements are not encouraged for at least six days. Visitors are also discouraged if possible. On the third postoperative day, the dressing is changed and the position of the graft and sutures is determined. The graft is hazy and swollen at this time, from imbibition of fluid through the incision and from the pressure of the sutures. The pupil, if mobile at the time of operation, is now small; 10 per cent phenylephrine hydrochloride (neo-synephrine hydrochloride®) and 5 per cent homatropine hydrobromide are instilled into the conjunctival sac, to prevent it from becoming fixed. If there is no obvious tendency for the graft to protrude, and the anterior chamber is satisfactorily reformed, the same loose binocular bandage is reapplied. However, if the graft bulges more than can be explained by simple corneal edema, a firm adhesive bandage is applied.

On the sixth postoperative day, the eye is again dressed, and the corneal sutures are removed. Several drops of a 4 per cent solution of cocaine are instilled into the conjunctival sac. If the patient is a child or a particularly uncooperative adult,

general anesthesia is employed for removal of the sutures; chloroform is a good anesthetic for this short procedure. The upper lid is elevated and the patient asked to look down toward his feet while one arm of each suture is cut. The scissors are held with the points directed toward the top of the patient's head, so that an involuntary upward movement on his part can only cause the suture to slip off the tip of the scissors blade. The knot of each suture is then grasped with the small toothless forceps and the sutures are removed. A mild pressure bandage is then applied to the eye operated on, using long strips of adhesive tape that have been "flamed" to insure their sticking to the skin. The skin on that side of the face is first painted with tincture of benzoin U. S. P., which protects the skin and makes the adhesive tape adhere better. A cathartic is given on the sixth night, followed, if necessary, by an enema the next morning.

The bandage is subsequently changed every third day, pressure on the eye being increased with each dressing. The intact eye is left open on the third dressing and the patient allowed to sit up in bed. After the fourth dressing, he is allowed to sit in a chair beside the bed. The pupil is dilated during each dressing. After the fifth dressing, the patient is allowed bathroom privileges and may walk about. The pressure dressings are continued as long as there is any tendency of the graft to bulge; this is determined by examination with the slit lamp after the bandage is left off for an hour or two. The pressure dressings are maintained for at least three weeks, and often five or six weeks in case of keratoconus. The patient is usually allowed to go home after three weeks, even though the pressure dressing is still used. The visual acuity may be casually tested after three weeks, but refraction is not worth while for approximately two months.

#### COMMENT

*Corneal Trephines.*—A considerable amount of the research on corneal transplantation has been devoted to the development of corneal trephines. The goal has been the production of a trephine that would cut the entire incision into the anterior chamber in one operation. This problem has been approached in three general ways: (1) by increasing the speed of the incision, by means of mechanical trephines; (2) employing a trephine with a "guard," to hold the incised cornea in position and avoid loss of the anterior chamber until after completion of the incision, and (3) by "punching out" the entire corneal disk, in the manner of a paper punch. Illustrative of the last method is the "punch" devised and advocated by Wiener and Alvis.<sup>9</sup> The use of this type of instrument necessitates an additional incision into the anterior chamber for insertion of the lower arm of the punch; for this reason, the "punch" type of corneal trephine has never enjoyed wide use.

**Mechanical Trephines:** A number of mechanical trephines have been devised: first, trephines driven by a spring mechanism incorporated into the handle of the instrument (von Hippel,<sup>1</sup> Elschnig<sup>2</sup> and Filatov<sup>3</sup>), and, more recently, those driven by electricity. Representative of the first type is the Green trephine; this is an enlarged form of the

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9. Wiener, M., and Alvis, B. Y.: Transplantation of Cornea by Means of a Mechanically Obtained Beveled-Edged Segment, *Am. J. Ophth.* **23**:877-881, 1940.



earlier Green trephine used in operations for glaucoma. Green<sup>10</sup> claimed that this instrument will cut the entire circular incision into the anterior chamber at one time and did not mention the use of scissors in his operative procedure. Katzin<sup>11</sup> has recently endorsed this trephine, stating that over 90 per cent of 300 grafts were cut completely with the trephine alone. The most modern of the mechanical trephines is electrical; a circular blade is inserted into the hand piece of a dental drill (fig. 3). The remainder of the apparatus consists of a table dental power setup, with a foot control. In my experience, complete incision of the cornea with the electric trephine can seldom be performed. It is true that a larger portion of the circular incision can be carried down into the anterior chamber than is usually accomplished with the manual trephine. Against this small advantage, however, are the disadvantages of (1) an unwieldy and more complicated apparatus, (2) increased danger of injury to the lens and (3) the obvious need for frequent practice by the occasional operator.

It appears that the advocates of the mechanical trephines have overlooked one factor. In addition to the speed of rotation of the trephine, for which advantage they endorse the electrical and spring-driven instruments, the "normal" position of the trephine in relation to the cornea is of great importance in attempting a complete incision. Indeed, it is impossible to make a complete incision with any instrument unless it is held very close to a 90 degree angle with the apex of the cornea, and this is difficult to accomplish. The necessary increase in bulk and weight of the mechanical trephines make this optimal position only more difficult to attain.

**Trephine with a Guard:** Representative of the second group of trephines is the Paton type, which is a hand instrument with an encircling collar that can be fixed at varying distances above the cutting edge. Paton<sup>12</sup> stated that the graft can be completely excised with this trephine, eliminating the use of scissors. Contrary to his experience has been that of Franceschetti,<sup>13</sup> who admits that he is unable to cut a complete graft, even though he employs the superlative Franceschetti trephine made by Grieshaber.

The adjustable collar, or guard, was added to the corneal trephine with the idea that it would hold the cut edges of the incision together,

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10. Green, M. I.: A Simple Technic for Corneal Transplantation, *Arch. Ophth.* **33**:150-152 (Feb.) 1945.

11. Katzin, H. M.: Contributions to the Technic of Corneal Grafting, *Arch. Ophth.* **37**:379-382 (March) 1947.

12. Paton, R. T.: Complications Encountered in Keratoplasty, read before the New England Ophthalmological Society, Jan. 15, 1947, *Am. J. Ophth.* **30**:1436-1439, 1947.

13. Franceschetti, S., in Foster, J.: An Oculist in Switzerland, *Brit. J. Ophth.* **32**:83-111, 1948.

avoiding loss of the anterior chamber until the entire periphery of the graft was incised. By the same mechanism, the collar is supposed to prevent too deep penetration of the anterior chamber and consequent injury to the lens. In practice, however, the aqueous escapes as soon as any portion of the incision opens into the anterior chamber, with

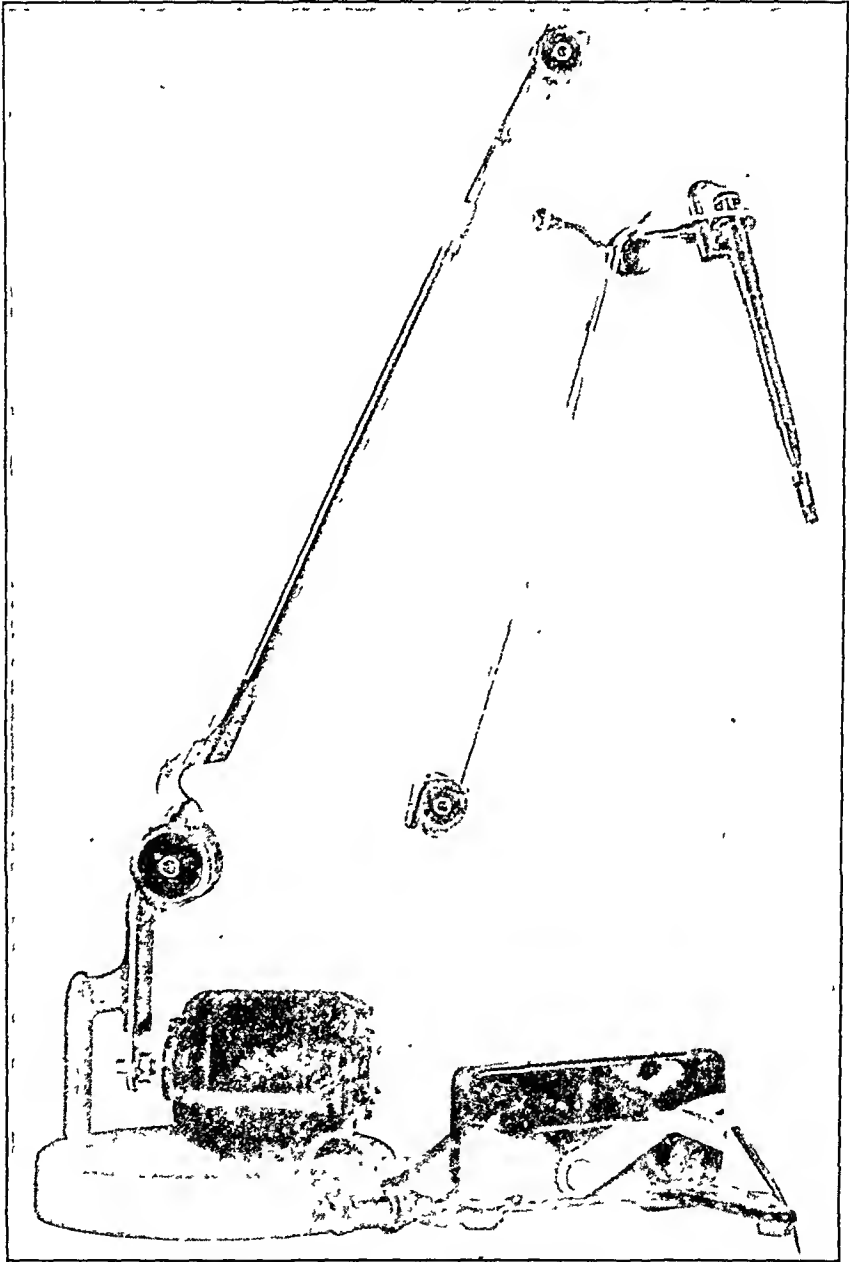


Fig. 3—Photograph of the electric corneal trephine.

this instrument just as with any other. The guard does not prevent the loss of aqueous through the outer edge of the incision; moreover, there is nothing to prevent loss of fluid from the inner side of the incision (into the trephine). Further, the guard does not prevent injury to the lens; when the anterior chamber is lost, the lens will come up against this trephine blade, as well as against any other.

**Manual Trephine:** In contradistinction to these three types of corneal trephines is the simple Elliott type of manual trephine (fig. 1, 2), which is twirled between the thumb and the fingers, just as in operations for glaucoma. This type of instrument has been used and recommended by Thomas,<sup>14</sup> Castroviejo<sup>78</sup> and others. This trephine is practical, both for marking the cornea and for making the incision. The instrument is light and easily held in the hand; the cutting edge is visible at all times. It is more likely to be applied to the cornea in a "normal" position because of these factors. It can be removed during the incision and reapplied in the same spot without any difficulty. Further, it is an instrument of simple pattern, easy to clean and to maintain. Considering that the much desired complete incision is not likely to be attained with any of the more complicated instruments yet devised, the simplicity of the manual trephine warrants its further employment.

**Sutures.**—The single continuous suture advocated by Castroviejo is an excellent one, in that it has loops of suture crossing the incision every 45 degrees of its circumference, producing the same effect as would four single sutures. However, it has the manifest disadvantage of being complicated; the several loops of this suture tend to get in the way during the operation and are often difficult to untangle at the end of the surgical procedure. In an attempt to simplify this aspect of the operation, the two sutures described under "Surgical Procedure" were tried, and they proved eminently satisfactory. Thomas<sup>14</sup> used these sutures in England and called them "criss-cross" sutures. Considering the number of investigations in this field in the past one hundred years, it is likely that some one may have used such a simple scheme before Thomas (at any rate, he makes no claim of priority for them).

Comparison of the "criss-cross" sutures with the single, continuous suture of Castroviejo reveals the following advantages:

1. The "criss-cross" sutures necessitate only four bites into the cornea, as compared with five bites for the continuous suture.
2. They offer less interference during the operation. Figure 4 is an artist's drawing of the location of these two sutures during the surgical procedure.
3. They are easier to draw up and tie. There are only two loops of suture with this method, and either one can be tightened at either end, and likewise tied at either end of the suture.
4. They are easier to remove after operation. It is necessary only to cut each suture once (at any place) and the entire suture can be removed in one piece, by traction on the knot.

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14. Thomas, J. W. T.: The Technique of Corneal Transplantation as Applied in a Series of Cases, *Tr. Ophth. Soc. U. Kingdom* **55**:373-392, 1935.

5. They are as effective as the single, continuous suture. There are eight loops of suture crossing the incision, 45 degrees apart, just as in the single, continuous suture. Viewed from a functional point of view, the two methods of suture hold the graft in place by identical means.

The principal advantage claimed for the single, continuous suture is that one can distribute the tension evenly throughout the suture by lifting under the central crossing point of the loops with a spatula at the end of the operation. This has not proved true in my experience. Considerable resistance is encountered when a suture is pulled through the corneal stroma by traction applied at right angles to the intracorneal segment. This resistance increases as the angle of trac-

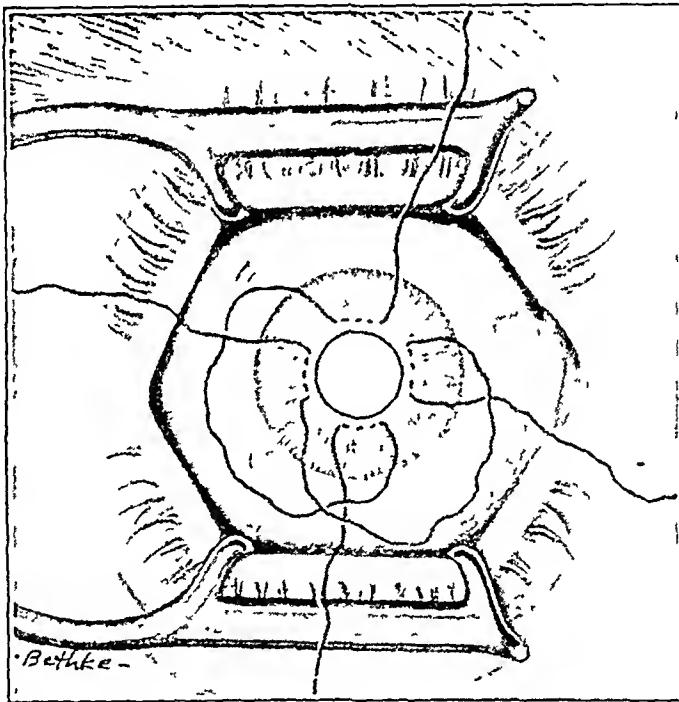


Fig. 4.—Artist's drawing showing the two corneal sutures as they appear during the surgical procedure.

tion becomes more acute, so that, at a 45 degree angle, the suture will cut through the cornea rather than slide through the corneal canal. Those who advocate this procedure are suggesting that they can overcome this resistance at four 90 degree angles and at four 45 degree angles, simultaneously, with only the force of a gently lifted spatula. Simple experiments will demonstrate that this is impossible:

1. Take an enucleated globe and make a round or square mark in the epithelium, as in corneal transplantation. Place the first corneal bite from 9 to 7 o'clock, as in the single, continuous suture, and attempt to draw the suture through the cornea by pulling at a 90 degree angle to the intracorneal segment of the suture. A surprising amount of

force is required. Then try to draw the suture through the cornea with traction at 45 degrees to the intracorneal segment; this is more difficult, and the force required will usually cause the suture to cut through the cornea.

2. Then place the second bite in the cornea from 1 to 12 o'clock, as in a keratoplasty, and attempt to pull the suture through the two corneal canals at the same time, by traction toward 6 o'clock (the normal direction of pull of this loop). It is impossible to do so. At this point, one is trying to draw the suture only through one 90 degree and two 45 degree turns. Placing the remaining three corneal bites (as in the completed single suture) will only add to the difficulty. Careful study of the Castroviejo suture will show that this resistance would have to be overcome both at all four 90 degree turns and at all four 45 degree turns, at the same time, for the proposed redistribution of tension to occur.

There is also clinical confirmation of these statements for those who are acquainted with the single, continuous suture. Those who have employed this suture will remember occasions on which at post-operative dressings one or more loops of the suture have been found loose and the others normally taut. Some will also remember instances in which one loop has cut through the cornea and lies free in the conjunctival sac, while the rest of the suture lies in its expected position. These findings can be explained only by the admission that a suture does not readily slide through the corneal stroma.

With any corneal suture involving sharp angles, therefore, it would appear more feasible to adjust the tension in the suture to the desired amount at the time of tying. After the suture is tied, tension can be effectively redistributed only by means of forceps at both ends of a buried segment and exertion of traction in one direction or the other.

*Additional Sutures.*—Occasionally, the final suture pattern will be asymmetric and the graft will bulge at some point. If the bulging is slight, it is better not to interfere. The sutures are not the only factor holding the graft in place; the pressure of the lids and of the bandage is of equal, or even greater, importance. However, if the bulge is alarming, it may be impossible to resist placing an additional suture. Direct coaptation of the wound edges with a suture at the site of the bulge is possible surgically, but this procedure is always unsuccessful because the suture subsequently pulls the graft toward the extra suture and causes a dehiscence in the wound directly opposite. A suture extending across the whole cornea, from limbus to limbus, so that it passes over the bulge and compresses it, has been found more successful.

*Evaluation of the Circular and Square Types of Corneal Grafts.*—Castroviejo<sup>75</sup> cited seven advantages of the square graft as compared

with the round transplant: (1) It is easier to bevel the graft and the cornea of the host; (2) the wound edges made by a trephine are irregular, and those made by a trephine-scissors combination are still more irregular; (3) completion of the round incision with scissors becomes progressively more difficult as the diameter of the circle diminishes; (4) the blades of the double-bladed knife are more easily tested and replaced than those of trephines; (5) the double-bladed knife offers more flexibility than does the trephine; (6) for grafts of different sizes, trephines of different diameters are needed, while the double-bladed knife is adjustable for all sizes of grafts, and (7) the latter instrument can be used to outline several grafts from the same donor eye (one, two, three or four square grafts from one cornea).

In refutation of these arguments, the following facts are offered, in the corresponding order:

1. Beveling of the graft or of the window in the host eye is not necessary, because the contraction of Descemet's membrane provides an automatic bevel in the graft, and because it is impossible to cut out the window in the recipient eye without a slight bevel posteriorly.

2. It is difficult to see why a straight knife should cut a cleaner incision than a curved one, provided that the instruments are equally sharp. The usual trephine incision in the cornea is sharp and symmetric. In regard to trephine-scissors combinations, it should be pointed out that the trephine cuts nearly the entire incision through the corneal stroma, leaving only a few corneal fibers, together with Descemet's membrane and the endothelium, to be severed with the scissors. On the other hand, the incision made by the double-bladed knife is only superficial; it cannot be carried deep into the cornea and still remain within the boundaries of the square. Therefore, most of the incision in making the square type of transplant must be made with scissors. It is incredible that a cleaner incision can be made by the crushing action of scissors than by the cutting action of a trephine.

3. It is true that the circular incision becomes more difficult as the circle becomes smaller, but it is equally true that the square incision increases in difficulty with smaller squares.

4. It is difficult to understand how the double-bladed knife can be tested in the same manner as a cataract knife. It is granted that the blades of the double-bladed knife are cheaper to replace than a trephine blade, but it is easier to change the blade of a trephine than the razor blades of the knife.

5. It is true that the double-bladed knife is more flexible than the trephine; that constitutes one of my main objections to the instrument.

6. It is granted that the double-bladed knife is better suited to preparation of different sizes of transplants.

7. It is impossible to concede that three or four square grafts can be cut from the same donor cornea. This would be technically difficult; there would be great differences in thickness in each graft, and, most pertinent of all, the cornea is not large enough.

To me, the circular type of corneal transplant appears more desirable than the square type; the following factors serve as the basis for this opinion:

1. Marking the cornea is easier with a trephine than with the double-bladed knife. A perfect circle can be expected with the corneal trephine, while a perfect square is difficult to obtain with the double-bladed knife. The razor blades in the double-bladed knife are flexible and tend to separate when applied to the cornea; thus the resulting pair of incisions may not be parallel. Often the second pair of lines is not made exactly at right angles to the first pair, and a parallelogram instead of a square is the result; moreover, the chances of cutting an identical parallelogram in the other eye are not very great. Further, with the double-bladed knife, it is possible to cut too deep at some point in the square (it is impossible to cut a straight incision with a constant depth in the curved cornea), allowing the cornea to bulge at this weakened focus and become distorted; or one blade of the knife may miss the cornea entirely at some point, leaving a defect in the fluorescein-stained figure. It is difficult to reapply the double-bladed knife in this instance.

2. Placing the sutures is a little more difficult in the circular type of operation. The corners serve as points of reference in the square operation, and the surgeon has only to estimate the halfway points between the corners. Symmetric location of the sutures in the circular operation may be attained with practice, however, and exact symmetry is not so important in this type of transplantation, where there are no corners to hold down.

3. Completion of the incision with scissors is easier with the circular operation, where there is only one incision, with one beginning and one ending. With the square form of keratoplasty, there are four separate incisions to make with scissors and four difficult corners to cut out. At each corner of the square transplant, there are two borders to the incision: one parallel to the cornea, and one at right angles to the corneal surface. The latter is the one that causes trouble; if one "overcuts" the corner in order to carry a true square down through Descemet's membrane, he may cut the suture (which is only 1 mm. away). The depth of corneal tissue to be severed with scissors in the circular operation is very slight, but in the square type of keratoplasty most of the thickness of the cornea is cut with scissors (particularly at the corners).

4. A better fit of the graft into the window in the host's cornea is obtained with a circular transplant because of factors 1 and 3. Mainly because it is possible to mark out two identical circles with the trephine, but also because the incisions can be more accurately completed with scissors, the circular graft will usually fit better than the square type.

5. Less astigmatism is found after operation with the circular form of transplantation. This can probably be attributed to the tendency of the corners of square transplants to bulge.

6. A better cosmetic result is generally conceded to the circular type of operation, where a thin scar may be almost imperceptible against the normal markings of the iris. This factor is not nearly so important, however, as factor 5.

#### CONCLUSIONS

1. A simplified, surgical procedure for use of circular, penetrating corneal transplants is described.

2. Various types of corneal trephines are discussed and evaluated. The simple, manual, Elliott type of instrument is recommended.

3. A simple method of suturing the graft in place is presented and is compared with the single, continuous suture formerly used.

4. The addition of extra corneal sutures in case of a bulging graft is briefly mentioned.

5. The circular type of corneal transplant is compared with the square type. The conclusion is reached that the circular graft is technically easier to accomplish and that the results with it are visually and cosmetically better.

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## ATROPHY OF THE OPTIC NERVE IN TABES AND DEMENTIA PARALYTICA

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THE PROBLEMS of atrophy of the optic nerve in syphilitic diseases have received new stimulation through the valuable work of Bruetsch.<sup>1</sup> Since I am one of the few investigators in this field who has had the opportunity to examine a rather large anatomic material, I should like to discuss some of these problems.

### INCIDENCE OF ATROPHY OF THE OPTIC NERVE IN TABES AND DEMENTIA PARALYTICA

On the basis of the ophthalmoscopic picture alone, according to various statistics, optic nerve atrophy exists in 5 to 10 per cent of cases of dementia paralytica and in 15 to 20 per cent of cases of tabes. The figures are entirely different if one counts the cases in which anatomic examination shows a typical degeneration of the peripheral optic pathways and the cases in which the degenerative process is still in an early stage. I found degeneration of the visual pathways in 16 of 53 cases of dementia paralytica, in all of 5 cases of the tabetic form of dementia paralytica and in 11 of 27 cases of tabes, an incidence about twice that in the clinically detected cases.

The percentage in Stargardt's<sup>2</sup> studies was even higher. In 8 of his 24 cases of dementia paralytica (examination was made only in very few cases of the tabetic form of the disease and of tabes) the visual pathways were normal, and in all the others there was some degree of degeneration.

Bruetsch's<sup>1</sup> observations were similar, and he expressed his belief that the discrepancy between clinical and anatomic findings is due to the fact that in the era before the advent of malaria therapy dementia paralytica, in contrast to tabes, was a fatal disease within an average of one to three years. Furthermore, the patient with dementia paralytica is often not able to recognize his visual failure; and, certainly, in large hospitals for mental disease examination by an ophthalmologist was

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The work of Mrs. Hoffman was supported in part by a grant from the American Cancer Society.

1. Bruetsch, W. L.: Malaria Therapy in Syphilitic Primary Optic Atrophy, *J. A. M. A.* **130**:14 (Jan. 5) 1946; *Tr. Am. Neurol. A.* **72**:129, 1946; Unilateral Syphilitic Primary Optic Atrophy, *Arch. Ophth.* **39**:80 (Jan.) 1948.

2. Stargardt, K.: *Arch. f. Psychiat.* **51**:711, 1913.

not made often. A third, and most interesting, point is that even in the presence of dementia paralytica and tabes the disk may look normal despite a certain degree of degeneration throughout the optic nerve (cases 4, 15, 16, 17, 21 and 22 of Stargardt<sup>2</sup>). This is contrary to the former belief that the ophthalmoscopic aspect of a pale disk is always the earliest symptom of optic nerve atrophy in tabes. There is no doubt, however, that pallor of the disk may be present even though the patient is not aware of visual failure.

PATHOGENESIS OF PRIMARY ATROPHY OF THE OPTIC NERVE  
IN TABES AND DEMENTIA PARALYTICA

Although the clinical entities dementia paralytica and tabes in their pure form are very different, the clinical course of optic nerve atrophy

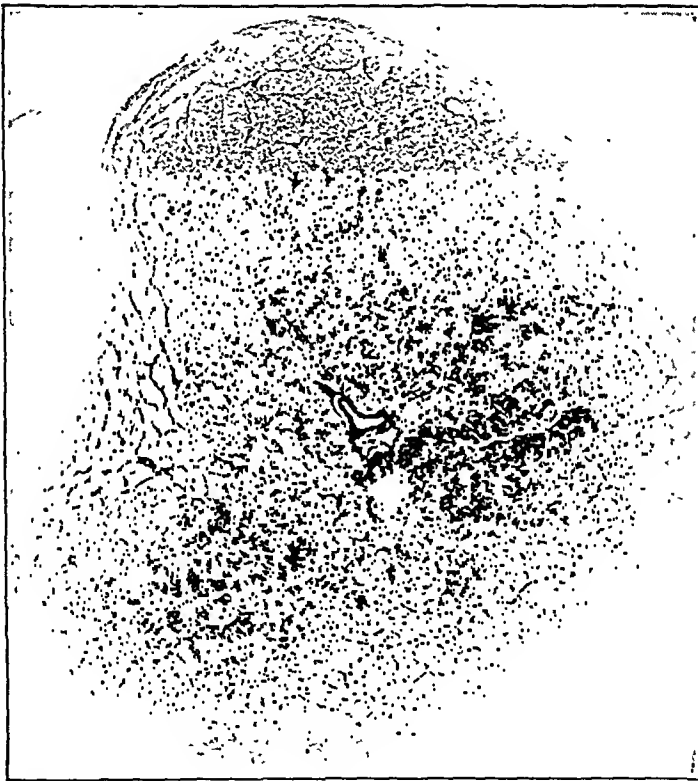


Fig. 1 (case 1).—Retrobulbar part of optic nerve in a case of tabes.

and its resistance to antisyphilitic drugs are similar in the two conditions, and one feels justified in considering the pathogenesis of the degeneration of the optic nerve in these two diseases on the same basis. This is not so with descending optic nerve atrophy in basilar syphilitic meningitis, and it was confusing when Bruetsch<sup>1</sup> proposed using the term primary syphilitic optic nerve atrophy for the degeneration of the optic nerve in all kinds of syphilitic disease of the central nervous system. This simplification is not in accordance with clinical and anatomic facts. In basilar meningitis with involvement of the intracranial portion of the optic nerves or optic chiasm the degeneration of the optic nerve is

“secondary” to an intense inflammatory infiltration, and the pallor of the disk sets in long after the visual disturbances; if the process is not too far advanced, antisyphilitic treatment has a prompt effect.

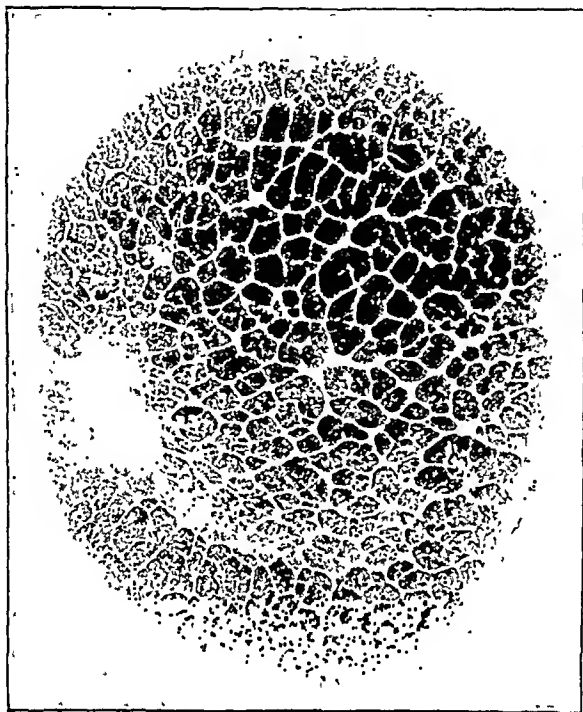


Fig. 2 (case 1).—Retro-orbital part of optic nerve in a case of tabes.



Fig. 3 (case 1).—Intracranial part of optic nerve in a case of tabes.

The pathogenesis of primary optic nerve atrophy in tabes and dementia paralytica is in many ways still a riddle. However, the anatomic investigations have not been in vain, and certain observations cannot be neglected in any attempt to explain the pathogenesis.

(a) *Origin of Degeneration at Periphery of Nerve.*—There is general agreement that the degeneration always starts at the periphery, adjacent to the pial sheath; the pathologic agent, therefore, always enters the nerve from the pia.

This being accepted, the following 2 observations are of special interest. As shown in the illustrations, in the case of tabes there was characteristic degeneration of the papillomacular bundle, which was located retrobulbarly at the periphery of the nerve, whereas more posteriorly, especially intracranially, the degeneration was in the center of the nerve (figs. 1, 2 and 3). It is noteworthy that the optic nerve of the other eye did not show degeneration of fibers but that there was about the same, rather pronounced, lymphocyte and plasma cell infiltration in the intracranial portion of the two optic nerves.

In the second observation (a case of dementia paralytica) the degeneration was most pronounced in the retrobulbar portion of the optic nerve and faded away more posteriorly (figs. 4, 5 and 6). Besides this pronounced degeneration there was a second (small) area, separate from the larger one. In the intracranial portion there was moderate infiltration of the optic septums, without any connection with the atrophic area.<sup>3</sup>

These two observations are of importance because they seem to prove that the starting point of the primary optic nerve atrophy may be in the retrobulbar portion of the nerve, and that the assumption of Stargardt,<sup>2</sup> Bruetsch<sup>1</sup> and others, namely, that the process always begins intracranially, does not conform with the facts. I do not wish to deny that in other cases the degeneration may start near the chiasm, but as yet there is no real proof. It is also possible that the process may start in the intracanalicular portion of the nerve. I have even seen localized atrophic changes in this region several times, but I am not sure whether they would have developed into the typical optic nerve atrophy of tabes.

(b) *Relation of Degeneration of Optic Nerve Fibers to Cellular Infiltration in Pia and Neighboring Septums.*—Bruetsch took it for granted that the degeneration was caused by inflammatory processes, relying on his own observations, as well as on the authority of Stargardt.<sup>2</sup> Stargardt no doubt was inclined to believe that the degeneration of the optic nerve of tabes and dementia paralytica always starts near the chiasm and that the exudative process plays a great role. But his statements are somewhat controversial. He stated<sup>4</sup> that there is no degeneration of a nerve fiber if there is not somewhere in its course an inflammatory process. Elsewhere,<sup>5</sup> he asserted that exudative and degenerative

3. More details on these cases are given in my monograph (*Syphilis und Auge*, Berlin, Julius Springer, 1928, p. 370).

4. Stargardt,<sup>2</sup> p. 904.

5. Stargardt,<sup>2</sup> p. 936.

processes are independent of each other but that they have the same source.

In my studies I found degeneration and exudation in some cases and degeneration or exudation alone in others.<sup>6</sup> A most convincing demonstration of how independent of each other these two pathologic reactions can be is presented: Anatomic examination of an optic nerve from a case of dementia paralytica in my collection showed a marginal area passing through the optic nerve and chiasm which could be stained only with osmic acid (Marchi method). This Marchi degeneration is always

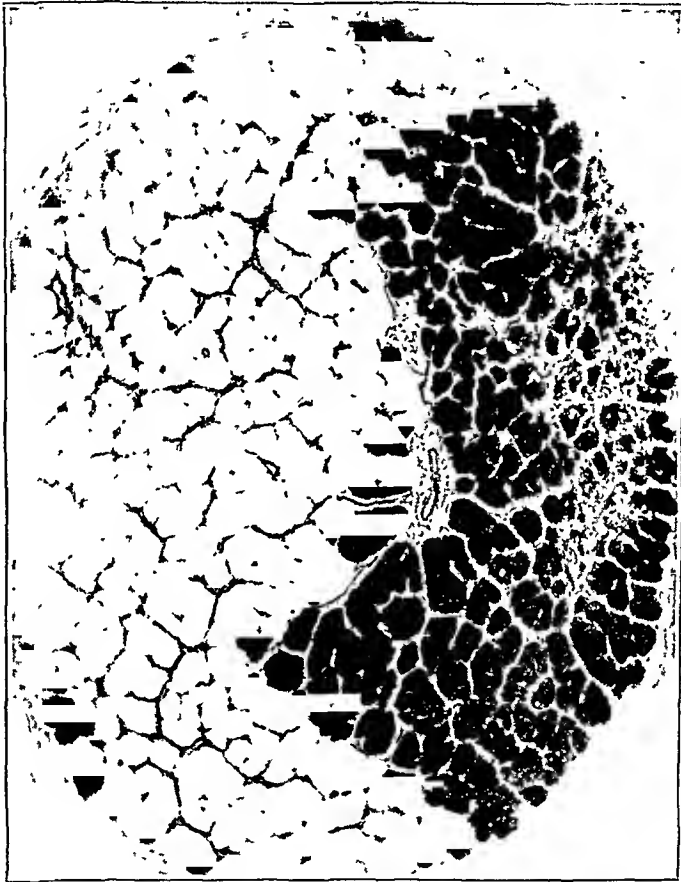


Fig. 4 (case 2.)—Retrobulbar part of optic nerve in a case of dementia paralytica.

a sign of a degeneration not older than about two months. This case is probably the earliest instance of an anatomically examined area of primary degeneration which exists in the literature. Throughout the length of this degenerated area there was no evidence of infiltration with lymphocytes or plasma cells! If the inflammation is really the *sine qua non* of the occurrence of degeneration in the optic nerve, it should have been present at such an early stage.

6. Igersheimer, J.: Jahresb. u. d. ges. Ophth. 48:225, 1924; Deutsche med. Wchnschr. 52:943, 1926.



Fig. 5 (case 2).—Retro-orbital part of optic nerve in a case of dementia paralytica.

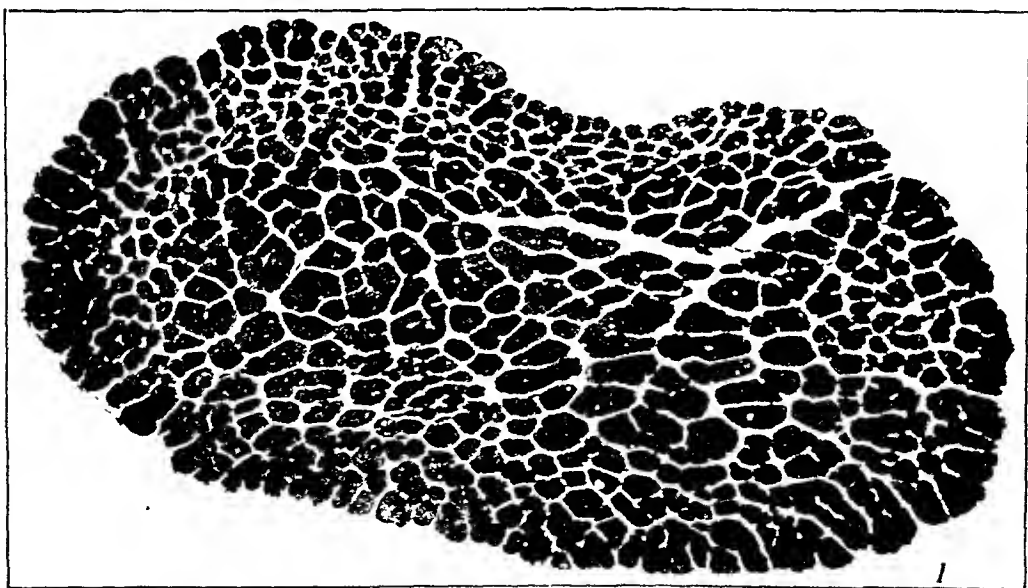


Fig. 6 (case 2).—Intracranial part of optic nerve in a case of dementia paralytica.

Behr<sup>7</sup> made the same observation as I. Even among Stargardt's published cases there were a number in which a marked discrepancy between the occurrence of degeneration and of exudation appeared. Bruetsch saw inflammatory changes in the intracranial portion without degeneration, but apparently not the reverse. How many of his patients had dementia paralytica and how many meningovascular syphilis is not mentioned; a case of pure tabes was apparently not in his material.

(c) *Treponemes and Optic Nerve Atrophy*.—I found treponemes in the leptomeninges in 1 case of tabes, in 2 cases of the tabetic form of dementia paralytica and in 7 cases of dementia paralytica. Two points must be stressed: 1. The organisms were located in the arachnoid, the pia and sometimes the marginal septums, but never in the neural parenchyma. 2. They were observed with inflammatory changes and, more frequently, with degenerative signs in the nerve, but never in the normal nerve of a person with tabes or dementia paralytica. It is, of course, regrettable that the number of positive results was not greater, but anyone who has done any staining and searching for spirochetes will understand this.

#### SUMMARY

In any attempt to explain the pathogenesis of atrophy of the optic nerve in tabes and in dementia paralytica, the following points should be borne in mind:

1. The pathologic process in the optic nerve in these diseases always starts in the marginal zone, near the pial sheath, and therefore the causative agent enters from the meninges.

2. Degeneration has been seen in the earliest stages, without any signs of exudation; on the other hand, degenerative and infiltrative processes exist together, and inflammatory signs in the intracranial portion of the nerve are frequently present without any atrophy.

3. The treponemes in the cases in which they could be found were always located in the arachnoid and pia of the optic nerve, and never in the neural parenchyma.

4. Antisyphilitic drugs, such as arsenicals or bismuth preparations, generally have no healing or arresting effect on the optic nerve atrophy in tabes and dementia paralytica, whereas they may influence descending optic nerve atrophy in basilar meningeal syphilis. Why malarial treatment has better results in primary syphilitic atrophy of the optic nerve is not yet known; certainly, it cannot be explained by its effect in decreasing the infiltration and therefore arresting the degeneration.

Behr's<sup>7</sup> attempt to explain the pathogenesis of the various types of syphilitic optic nerve atrophy is a hypothesis based on these facts, but,

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7. Behr, C.: München. med. Wchnschr. 73:366, 1926.

of course, still a hypothesis. According to his concept, basilar syphilis is a disease of the mesodermal tissue, and the optic nerve atrophy is due to a syphilitic optic neuritis involving the intracranial portion of the nerve. There is an infiltration of the septums, especially around the small vessels, with subsequent nutritional disturbances of the nerve tissue. The nerve tissue, reduced in its resistance, is further damaged by toxic products of the treponemes. Antisyphilitic drugs, if they are not used in too late a stage, clear up the nutritional difficulties, with resulting improvement in the visual disturbances. The pathologic process in the optic nerve associated with tabes and dementia paralytica, however, may start in any part of the nerve. Inflammatory signs do not play an important role. Two kinds of changes are important. The one concerns the septal system. Part of the fine septums is destroyed, and with them the nourishing capillaries; another part becomes shortened and thickened. Still more important are structural and chemical changes in the glial system. As this system is the main factor in normal nutrition of the nerve tissue, the changes in the glia and the disappearance of capillaries are considered the cause of the degeneration of the nerve fibers and of the irreversibility of the process with treatment. The pathologic process is due to the effect of the undetermined toxins of the treponemes.



## SURGICAL TREATMENT OF CONCOMITANT DIVERGENT STRABISMUS

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AND

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THE SURGICAL treatment of concomitant exotropia is said not to be as satisfactory as that of esotropia. This does not seem to be true, but it is difficult to predict the exact result of an operation, since the outcome is variable even when the operation is performed by the same surgeon employing the same technic.

Lancaster<sup>1</sup> stated that theoretically in correction of squint of lesser degree a 1 mm. movement of muscle insertion should shift the eyeball 2 degrees. Jameson<sup>2</sup> and Chavasse<sup>3</sup> advocated 1 mm. of recession of the lateral rectus muscle for each 2 degrees of correction desired, but Gifford<sup>4</sup> stated that 1 mm. of recession of the lateral rectus results in an average of only 1.5 degrees of correction.

In an effort to determine the average amount of correction resulting from certain operative procedures, statistics were compiled from 49 consecutive cases, in each of which the patient had been observed for more than one year after operation.

Divergent squint developed in the majority of patients after the age of 6 years, in contrast with the convergent type. The age of onset was at 6 years or more in 60 per cent of patients and under 6 years in 40 per cent.

Fixation varied, as it does in convergent squint, being alternating in 58 per cent of patients and monocular in 42 per cent.

Visual acuity was 6/9 or better in each eye in 55 per cent of patients and 6/30 or less in one eye in 18 per cent. Only 3 eyes showed

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1. Lancaster, W. B., in Berens, C.: *The Eye and Its Diseases*, Philadelphia, W. B. Saunders Company, 1936.

2. Jameson, P. C.: *Entity of Muscle Recession: Short Résumé of Its Technic and Principles with New Supplementary Notes and Illustrations*, Arch. Ophth. **21**: 362 (Feb.) 1939.

3. Chavasse, F. M., in Worth, C.: *Worth's Squint*, revised by F. B. Chavasse, ed. 7, Philadelphia, P. Blakiston's Son & Company, 1939.

4. Gifford, S. R.: *A Textbook of Ophthalmology*, Philadelphia, W. B. Saunders Company, 1938.

a pathologic condition interfering with visual acuity, 2 having scarred corneas and 1 a macular lesion. In 37 per cent of patients the visual acuity differed in the two eyes at least two lines on the Snellen chart.

Hypermetropia in each eye was present in 60 per cent of patients, but only 1 showed more than 3.00 D. of hypermetropia and only 1 had anisometropia of over 2.00 D. Only 14 per cent of the patients were myopic in both eyes, and none had an error of over 2.00 D. Antimetropia (hypermetropia in one eye and myopia in the other) was found in 26 per cent of these patients. Retinal correspondence was normal at first examination in 70 per cent of the patients and abnormal in 22 per cent and changed from abnormal to normal after orthoptic training in 8 per cent. Convergence insufficiency plus divergence excess was noted in 53 per cent of patients and divergence excess alone in 47 per cent. Patients with convergence insufficiency alone were not included in this study.

In 49 cases the operations were performed by one surgeon, employing the same technic; thus, results should be comparable. Three operations, alone or in combination, were employed, namely (1) recession of the lateral rectus muscle, (2) resection of the medial rectus muscle and (3) resection and advancement of the medial rectus muscle.

The great discrepancy in results following operations for concomitant divergent strabismus may be noted in the accompanying tabulations.

*Recession on Lateral Rectus Muscle of One Eye*

Squint, Degrees	Recession, Mm.	Correction, Degrees
0-10	5	4
(7 cases)	6	8
	5	6
	4	3
	6	10
	6	8
	5	8
	Average $\overline{5.3}$	Average $\overline{6.7}$

One millimeter of recession corrected an average of 1.2 degrees of squint.

11-20	5	5
(6 cases)	7	10
	5	16
	6	10
	5	10
	6	7
	Average $\overline{5.7}$	Average $\overline{9.7}$

One millimeter of recession corrected an average of 1.7 degrees of squint.

21 or more	5	13
(2 cases)	7	11
	Average $\frac{6}{\rule{1cm}{0.4pt}}$	Average $\frac{12}{\rule{1cm}{0.4pt}}$

One millimeter of recession corrected an average of 2 degrees of squint.

In looking over these figures, one is struck by the great variation in the results of similar amounts of recession. For example, a 5 mm. recession resulted in corrections of from 4 to 16 degrees! One does gain the impression that the greater the degree of squint the greater the correction after similar amounts of recession.

*Bilateral Recession of Lateral Rectus Muscle*

Squint, Degrees	Total Recession, Mm.	Correction, Degrees
10-20	11	13
(6 cases)	9	10
	10	8
	10	16
	10	6
	10	9
	$\frac{\rule{1cm}{0.4pt}}{\text{Average } 10}$	$\frac{\rule{1cm}{0.4pt}}{\text{Average } 10.3}$

Thus, 1 millimeter of recession corrected an average of 1 degree of squint.

These results are not comparable to those obtained with a unilateral recession, in which each millimeter of recession corrected an average of 1.7 degrees of squint.

*Resection of Medial Rectus Muscle of One Eye*

Squint, Degrees	Resection, Mm.	Correction, Degrees
0-10	8	8
(12 cases)	10	8
	10	2
	12	6
	8	10
	8	8
	10	8
	6	5
	10	2
	10	3
	5	9
	8	7
	$\frac{\rule{1cm}{0.4pt}}{\text{Average } 8.6}$	$\frac{\rule{1cm}{0.4pt}}{\text{Average } 6.3}$

Here, each millimeter of resection corrected an average of only 0.73 degree of squint.

This operation when used alone was more unpredictable in its results than was recession; e. g., 10 mm. of resection resulted in from 2 to 8 degrees of correction. Furthermore, it had less effect than any single operation.

*Recession of Lateral Rectus and Resection of Medial Rectus Muscle  
(on Same Eye and at Same Time)*

Squint, Degrees	Total Recession and Resection, Mm.	Correction, Degrees
11-20	15	12
(5 cases)	15	15
	15	16
	16	20
	8	12
	Average 14	Average 15
21-30	15	21
(3 cases)	15	9
	14	13
	Average 14.6	Average 14.3

Each millimeter of recession or resection corrected an average of 1 degree of squint.

Here, again, there is inconsistency in results; e. g., 14 mm. of recession and resection resulted in from 9 to 21 degrees of correction. However, most results were reasonably alike.

*Resection and Advancement of Medial Rectus Muscle*

Squint, Degrees	Resection and Advancement, Mm.	Correction, Degrees
10-20	R 5	
	7	10
(4 cases)	A 2	
	R 10	
	11	14
	A 1	
	R 5	
	7	6
	A 2	
	R 10	
	12	15
	A 2	
	Average 9.2	Average 11.1

One millimeter corrected an average of 1.2 degrees of squint.

*Recession of Lateral Rectus Muscle and Resection and Advancement of Medial Rectus Muscle (on Same Eye and at Same Time)*

Squint, Degrees	Recession Total Resection- Advancement, Mm.	Correction, Degrees
20-30	16	21
(6 cases)	15	17
	16	25
	12	25
	18	28
	18	23
	Average $\overline{15.8}$	Average $\overline{23.1}$

One millimeter corrected an average of 1.4 degrees of squint.

30 +	16	17
(4 cases)	18	39
	17	35
	20	36
	Average $\overline{17.7}$	Average $\overline{31.7}$

One millimeter corrected an average of 1.8 degrees of squint.

These results were perhaps the most consistent, although it is realized that in 1 instance a 15 mm. change in the muscles corrected only 17 degrees of squint, while in another case an 18 mm. change in the muscles produced 39 degrees of correction.

It is stated in the literature that one should recess the lateral rectus muscle in cases of divergence excess and that in correction of divergence excess plus convergence insufficiency the lateral rectus muscle should be recessed and the medial rectus muscle resected or resected and advanced. Theoretically, this reasoning is excellent and logical, but our figures do not bear out the necessity of differentiating the types of squint in order to choose the proper operation. Recession of the lateral rectus was equally effective in correction of each type of squint; resection of the medial rectus alone gave quite unpredictable results but was apparently just as effective in one type of squint as in the other. Results in cases in which a single operation was performed were as follows:

*Recession of Lateral Rectus Muscle*

	Recession, Mm.	Correction, Degrees
Divergence Excess	5	12
(7 cases)	5	4
	7	6
	4	2
	7	10
	5	16
	5	8
	Average $\overline{5.4}$	Average $\overline{8.3}$

One millimeter corrected 1.5 degrees of squint.

Divergence Excess	10	9
plus	6	10
Convergence Insufficiency	5	10
	Average $\overline{7}$	Average $\overline{9.7}$

One millimeter corrected 1.4 degrees of squint.

*Resection of Medial Rectus Muscle*

	Recession, Mm.	Correction, Degrees
	8	8
Divergence Excess	10	8
(4 cases)	10	8
	6	5
	Average $\overline{8}$	Average $\overline{7}$

One millimeter corrected 0.9 degrees of squint.

Divergence Excess	8	0
plus	10	2
Convergence Insufficiency	10	3
	8	7
	Average $\overline{9}$	Average $\overline{3}$

One millimeter corrected 0.3 degree of squint.

It may be stated that there was little apparent difference in the effect of an operation in cases of divergence excess and in cases of divergence excess plus convergence insufficiency.

*Relation of the Type of Squint to the Effect of Operation*

Deviation, Degrees	Divergence Excess No. of Cases	Correction (for Each Mm. Muscle)	Divergence Excess Plus Convergence Insufficiency	Correction (for Each Mm. Muscle)
0 - 10	5	0.7	6	0.64
11 - 20	11	1.1	6	1.0
21 - 30	4	1.3	9	1.5
31 - 45	1	1.4	5	1.6

One would expect that the results in patients with normal retinal correspondence would be better than in those with abnormal correspondence. Of the 38 patients with normal correspondence, 8 had undercorrection, with a residual exotropia of from 3 to 8 degrees, and 3 had overcorrection, 2 having 2 degrees of esotropia and 1 7 degrees. Two of 11 patients with abnormal retinal correspondence had undercorrection, 1 having 3 degrees and the other 16 degrees of exotropia; 1 patient had overcorrection of 1 degree. It seems that normal retinal correspondence is of no particular value so far as the result of operation is concerned, but it should help to keep the eyes in alinement.

Results are satisfactory in cases with abnormal retinal correspondence when the appearance of the patient is such that the squint

goes unnoticed. With 2 or 3 degrees of residual exotropia or esotropia the cosmetic result is good. In patients with normal retinal correspondence one desires parallelism, or only a low degree of residual exophoria. On the basis of these criteria, 10 of 49 patients had an undercorrection, i. e., an exotropia of 3 or more degrees (9 patients had from 3 to 8 degrees, and 1 patient with eccentric fixation had 16 degrees). Four of the 49 patients had overcorrection—1 patient had 1 degree of esotropia, 2 had 2 degrees and 1 had 7 degrees.

### CONCLUSIONS

Results of operations in concomitant exotropia appear to be extremely variable, even with a standard technic in the hands of the same surgeon.

If the operation is confined to one eye it is difficult to overcorrect the higher degrees of exotropia.

Retinal correspondence appears to have no bearing on the surgical result.

The exotropia of divergence excess and that of divergence excess plus convergence insufficiency apparently respond equally well to operation, and it is not necessary to differentiate the type of defect in order to decide on the operative procedure.

In correction of the moderate and higher degrees of divergent squint, it is advisable to make an operation on both the lateral and the medial rectus muscles at the same time. This is in contradistinction to the procedure for convergent squint, in which it is best to make a two stage operation.

In spite of the variable results, the following operations are advised:

Exotropia of less than 10 degrees: recession of the lateral rectus muscle in one eye (from 4 to 7 mm.). One should expect approximately 1 degree of correction for each millimeter of recession.

Exotropia of 11 to 20 degrees: recession of the lateral rectus muscle and resection of the medial rectus muscle on one eye. The amount of recession is 5 to 6 mm. and the amount of resection 6 to 10 mm. One should expect approximately 1 degree of correction for each millimeter of change in the muscles.

Exotropia over 20 degrees: recession of the lateral rectus muscle and resection and advancement of the medial rectus muscle on one side. The amount of recession is 5 to 6 mm., the amount of resection 6 to 10 mm. and the amount of advancement 2 to 3 mm. Approximately 1.5 degrees of correction may be expected from each millimeter of change in the muscles.

In any of these cases residual squint may be corrected by an operation on the opposite eye.

Department of Ophthalmology, State University of Iowa College of Medicine.

# CORNEAL VASCULARIZATION IN THE GRAY NORWAY RAT

IRVING H. LEOPOLD, M.D., D.Sc.

ELEANOR YEAKEL, Ph.D.

AND

LARRY L. CALKINS, M.D.

PHILADELPHIA

VASCULARIZATION of the cornea may be produced experimentally in animals by various means. Rabbits, dogs, rats and guinea pigs have been used with uniform success, and there is no evidence that a particular species or strain is more susceptible than another. Maintenance on a stock laboratory diet is generally accepted

## *Incidence of Corneal Vascularization*

Norway Gray Rats				
Age, Days	Number of Rats	Number of Rats with Vessels	Number of Eyes with Vessels	Percentage of Rats with Vessels
Up to 500.....	40	3	4	7.5
Over 500.....	39	19	29	48.7
Albino Rats				
Up to 500.....	26	0	0	0
Over 500.....	19	0	0	0

to be a safeguard against the spontaneous development of the condition. However, corneal invasion was discovered in a group of supposedly normal gray Norway rats that were not known to be suffering from any dietary deficiency or other pathogenic condition. Albino rats in the same colony were found to be free of corneal vascularization.

## METHOD

The rats were born and raised in the Wistar Institute animal colony and ranged in age from 64 to 766 days. Their diet consisted of Purina dog chow pellets ad libitum, and greens (principally lettuce) given twice each week. This diet is theoretically adequate for the nutritional requirements of the rat. The eyes of 23 male and 22 female Wistar albino rats, and 37 male and 42 female domesticated gray Norway rats were examined. The pupils were dilated with 2 per cent homatropine hydrobromide, and the corneas were observed with an ophthalmoscope. Light ether anesthesia was employed to immobilize the young gray rats only.

From the Department of Ophthalmology, Hospital of the University of Pennsylvania, and Wistar Institute, University of Pennsylvania.



## RESULTS

The data are presented in the accompanying table. Only 7.5 per cent of the gray Norway rats under 500 days of age, but 48.7 per cent of these rats over 500 days old, showed corneal vascularization. There was no significant difference in the incidence with respect to sex. None of the albino rats showed corneal vascularization at any age. The photomicrographs of the cornea of a Norway gray rat shows vessels in the midstroma.



Vessels in the midstroma of the cornea  $\times 125$ .

## COMMENT

The results indicate that corneal vascularization develops spontaneously in gray Norway rats, but not in Wistar albino rats, and that its incidence increases with age. Apparently, the two strains differ in susceptibility to the condition, but the cause of the difference is not known. Vascularization of the cornea can be brought about in many ways and by a variety of agents, both local and endogenous. Under the former may be listed bacteria, virus and protozoa; chemical agents, and burns. Endogenous agents include allergens; toxic material—that spreads from an inflammatory focus and stimulates capillary ingrowth.

and nutritional deficiencies, either from a restricted diet or from an increased demand of the organism.

Some of these causes can probably be eliminated in a consideration of the etiologic factor responsible in the gray rats. The gray Norway rat may differ from the albino rat constitutionally, i. e., it may be more sensitive to burns, bacteria, allergy or food deficiencies.

The spontaneous incidence in gray Norway rats of corneal vascularization of unknown origin makes these animals useful as subjects for investigation of the underlying causes and as test animals in experimental work requiring the production or presence of vascular invasion.

#### SUMMARY

Corneal vascularization occurred in the Norway gray rats, but not in the albino rats, when the two strains were maintained on similar diets and in the same colony. Sex had no influence on the incidence of the vascularization. The vascularization increased with age and was most pronounced in Norway gray rats over 500 days old.

## Clinical Notes

### A SIMPLE METHOD FOR TEMPORARY CLOSURE OF THE LIDS

DAVID G. COGAN, M.D.  
BOSTON

**I**N CASES in which it is desirable to close the lids for a few days to a few weeks, or occasionally as a preliminary to lid suturing, I have found "glueing" the lids together a useful procedure.

The cases in which I have employed this method have chiefly been those in which there were facial paralysis and corneal anesthesia, so that exposure keratitis was thought to be an imminent possibility. Among such cases were instances of facial paralysis following intracranial operation or trigeminal resection (for tic douloureux), in which it was thought that the facial paralysis was not to be permanent, or instances of facial paralysis and corneal anesthesia resulting from spontaneous but transient intracranial lesions (aneurysms). When the paralysis persisted more than a few weeks, the lids were subsequently sutured. I have also used the procedure in cases of coma in which there was an exposure keratitis from incomplete closure of the lids; in these instances, however, the procedure is preferable to taping only when the restlessness of the patient makes the taping unsatisfactory. In 1 instance the lids of one eye were glued together to avoid a diplopia for which a patch was too "bothersome."

The "glue" which I have employed is the standard Duco cement,<sup>®</sup> which is commercially available in hardware or variety stores. The procedure consists in closing the patient's eyes and applying by means of a tooth pick applicator several layers of the cement to the lashes of the upper lids, sealing them down to the cutaneous surface of the lower lid, at first 1 to 2 mm. below the margin of the lower lid. Time is allowed for drying of each layer, and subsequent layers are placed higher up so as to occlude ultimately the palpebral fissure and form a cast covering much of the upper and lower lids. The medial ends of the lids are not stuck together, however, so that tears and secretory products may drain out of the conjunctival cul-de-sac.

The cast provides a firm cohesion of the lids lasting 3 to 5 weeks. At first transparent, it may become partially opaque by reason of air bubbles within it; yet it is never conspicuous cosmetically. When it finally comes off, it may remove several of the cilia with it, but this is of no practical consequence.

The only complication I have encountered in the 10 cases on which I have used the method is a sensitivity reaction, in 1 instance. In this case there developed considerable swelling of the lids and redness on the seventh day following its application. The swelling promptly disappeared after removal of the cast, and the lids were then sutured. There is, of course, some danger of bringing the fresh cement in contact with the cornea, but if the substance is applied carefully and the lids are kept closed manually while the cement is being applied, this danger is negligible.

## A SIMPLE AND EFFICIENT CATARACT SUTURE

JOSEPH LAVAL, M.D.

NEW YORK

THERE are so many different types of cataract sutures in use that I hesitate to present still another. However, at the Manhattan Eye, Ear and Throat Hospital this one has proved very efficient and easily used as well as at the Mount Sinai Hospital, where the residents in ophthalmology have been using it.

There are several general classes of corneoscleral sutures: (1) the preplaced sutures, such as the Stallard, the MacLean and the Verhoeff; (2) sutures placed after the section such as the Kirby; (3) sutures placed partly before and partly after the section, such as the Castroviejo. The suture I present is a compromise between the preplaced suture and the suture placed after the section, the compromise consisting in making a small 5 mm. keratome section and then placing the suture. It is somewhat similar to the Perrera type.

After lid akinesia and retrobulbar injection of procaine, two silk sutures are placed in the upper lid, one in the lower lid and one through the superior rectus muscle, as a bridle suture. No speculum is used. A conjunctival incision is made 5 mm. from the limbus for one-half the circumference of the cornea (figure, *A*). The conjunctiva is undermined to the limbus, and the corneoscleral junction is exposed in the region of 12 o'clock.

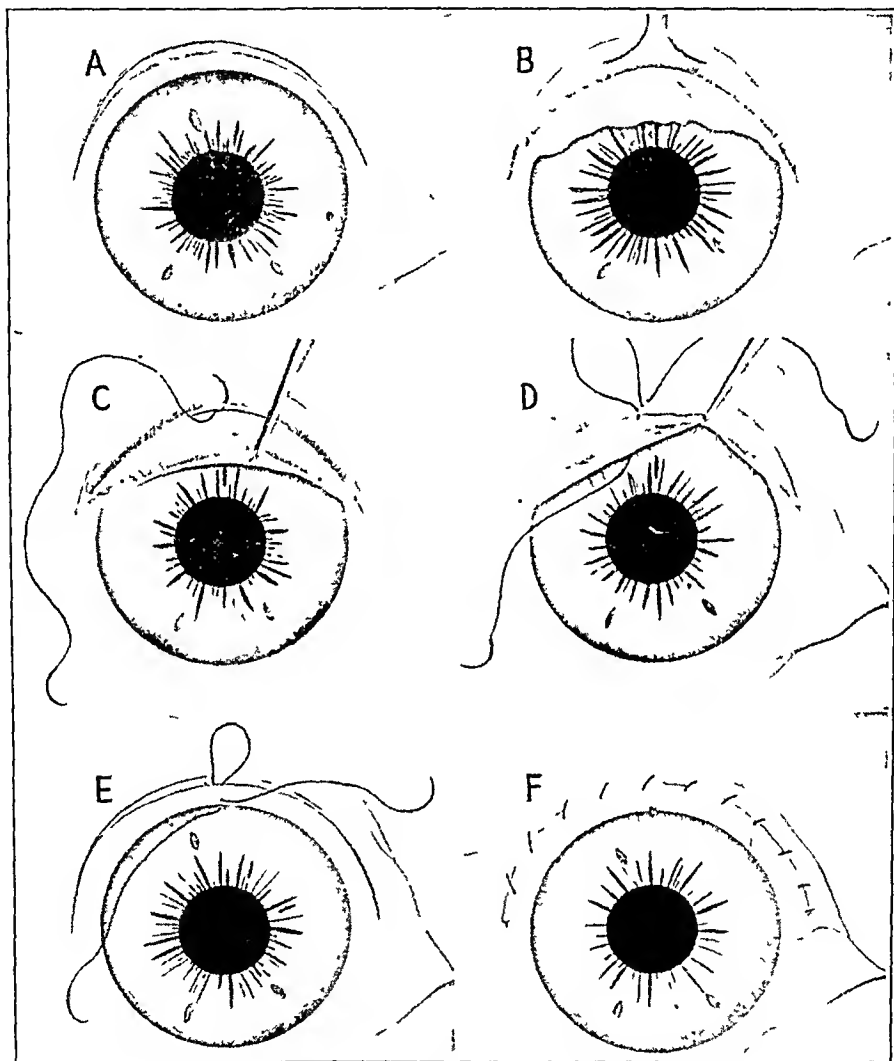
A keratome incision about 5 mm. long is made at this point (figure, *B*). One needle of a double-armed suture (000000 silk with a traumatic needle) is passed through the outer layers of the scleral lip of the keratome wound, the point of the needle facing the surgeon (figure, *C*). The other needle of the double-armed suture is passed through the corneal lip of the keratome wound, the needle tip facing away from the surgeon (figure, *D*). The first needle, which passed through the scleral lip, is now taken through the conjunctiva close to its attachment to the corneal lip, the tip of the needle facing away from the surgeon (figure, *E*). The suture is looped away from the wound and a loose tie taken. The section is enlarged with scissors. A peripheral or a complete iridectomy is performed, the lens is removed, and then the suture is firmly tied, the corneal and the scleral edges of the wound being brought snugly together. The conjunctival incision is closed by a running silk suture (000000), with a knot tied firmly at each end of the suture (figure, *F*). This gives good tight conjunctival closure. If the surgeon likes to put an air bubble into the anterior chamber, he does this after the conjunctiva has been closed. The patient is often

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Read at a meeting of the Section of Ophthalmology of the New York Academy of Medicine, Oct. 18, 1948.

sent from the operating room with the eye not operated on uncovered. He is allowed out of bed the day after the operation. Postoperative complications, such as prolapsed iris or hyphema, are extremely infrequent. Postoperative astigmatism is kept at a minimum.

I realize that most surgeons do not like to place cataract sutures after the section has been made. I believe that this objection is over-



Steps in placement of a new cataract suture.

come by making a 5 mm. keratome section and then placing the sutures before the section is enlarged. Grasping of the scleral and corneal edges of the wound with mouse-toothed forceps at this stage for insertion of the sutures is free of any hazards. I have never had any trouble or complications while doing it. The method has an advantage over use of the Kirby suture with conjunctival flap in that the suture is placed after a very small incision (5 mm.) has been made. It has one advantage

over the Verhoeff and MacLean sutures in that it is much more easily and more quickly placed. The possible advantage of the MacLean and Verhoeff sutures in that they may be placed before the section is made is more than counterbalanced by the difficulty encountered in making the section after the suture is in place. The only advantage of my method over Perrera's is that only one suture has to be placed, and I am firmly convinced that one good suture is enough. I must admit, however, that one objection can be made to my method; that is the theoretic possibility of an ever so slight malplacement of the corneal and scleral bites, so that the two lips of the wound are not in exact microscopic apposition. To my mind, however, that is a purely theoretic, and not a practical, objection.

136 East Sixty-Fourth Street (21).

## News and Notes

EDITED BY DR. W. L. BENEDICT

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### UNIVERSITY NEWS

**Research on Corneal Transplantation, Stanford University School of Medicine.**—Research on corneal transplantation will be carried out by Dr. Alfred E. Maumenee, head of the ophthalmology department at the Stanford University School of Medicine, under a contract with the National Advisory Council of the United States Public Health Service.

Dean Loren R. Chandler, of the medical school, in announcing receipt of the grant, said that the funds included an allowance for a research fellow and that applications for the fellowship are requested by the medical school.

The research grant is for one year but is subject to renewal.

### SOCIETY NEWS

**The American Ophthalmological Society.**—The officers elected at the recent meeting of the American Ophthalmological Society are Dr. Parker Heath, president; Dr. John H. Dunnington, vice president, and Dr. Maynard C. Wheeler, secretary-treasurer.

## Correspondence

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### COMMENTS ON DR. RAND'S LETTER ON HARTRIDGE'S ARTICLE ON PHYSIOLOGY OF VISION

*To the Editor:*—May I make a few comments on the review of some of my papers which Dr. Rand contributed to the October 1947 issue of the ARCHIVES, page 529? She refers to Granit's work on animals with the microelectrode and to my attempts to investigate the properties of the human retina, using an optical instrument called the retinal microstimulator. She states, "Hartridge utilized 'tenuous beams of light' sufficiently narrow to subtend at the eye an angle of only 8 seconds of arc and to form on the retina, he claims, geometric images equal to one-fifth cone unit. (One 'cone unit,' according to Hartridge, subtends an angle at the observer's eye of 41.236 seconds of arc)." This is quite true, but I have pointed out with great care that the diffraction of light and the residual aberration of the human eye must cause the light of which the retinal image is comprised to spread far beyond the boundaries of its geometric image, because no optical contrivance at present known enables an image to be formed on the retina which is smaller than that based on the wave theory of light. By a careful adjustment of the conditions, however, the retinal image may be made to look to the observer far smaller and more sharply defined than would be expected on the basis of optical theory alone. The diffraction pattern of a point source of light when it falls on the retina probably acts as an adequate stimulus for 20 foveal receptors, if not many more. It might be supposed, therefore, that this number of receptors at least would form a functional unit. How wrong this idea is may be gaged from the fact that most normal-sighted observers can recognize the letters of the alphabet when they subtend at the eye 5 minutes by 4 minutes of arc, that is, that the geometric images of the letters on the retina fall on roughly 45 foveal receptors. Now the diffraction patterns of the various parts of these letters must overlap one another at every point, causing a blur of light which spreads over probably more than 100 foveal receptors. It might be concluded, therefore, that the resolution of the letters would be impossible under such conditions. But this conclusion would be completely at variance with the facts, because resolution is found to be quite easy under the conditions mentioned; in fact persons who have good acuity can sometimes identify letters when they subtend at the eye half the aforementioned angles, in which case the individual black and white parts of the letters must have widths which correspond to less than 1 cone unit. These are the conditions I aim at when using the microstimulation apparatus, and they are not at variance with the diffraction theory of light. The results achieved show that diffraction is by no means the only factor so far as human vision is concerned, for the evidence available is in favor of the idea that the retinal image which is impaired by diffraction and the aberrations is repaired again by processes at present but little understood.



Thus, when an observer with good visual acuity examines a point source of monochromatic light by using the optimum part of his fovea, a diffraction pattern of that object is cast on his retina which, as previously explained, has a diameter equal to many cone units. But the processes of repair, which must take place somewhere between the retina and the perceptual centers of the brain, have the effect of reducing the apparent diameter of this image until it is little larger than 1 cone unit. There can be little doubt that repair is greatly assisted by the physical distribution of light in the retinal image. Calculation has shown that under ordinary conditions of vision if the intensity of illumination of the foveal receptor is 100, on which the center of the diffraction pattern falls, then the circle of cones around this central cone receives illumination equal to 10; the circle outside these cones again, receives illumination equal to 2; the next circle, less than 0.5, and so on. Thus the central receptor receives a much higher intensity of illumination than any of the other receptors.

With regard to the processes of repair referred to, the sharpening of diffuse contours has long been known and has been described as one of the attributes of simultaneous contrast.

Before passing on, one must refer to the practical aspect and consider how effective these processes of repair really are. Does the diffraction pattern ever stimulate adequately so small a retinal area that the nervous message to the higher centers comes from one receptor only? The answer is "yes," without any possibility of doubt. But this limitation is as a rule achieved only when many point sources, close to one another in cone units, are being looked at. In cases in which only one source is being examined, or in which other sources are also present but are many cone units apart, this sharp limitation is not achieved as a rule. But what is achieved quite easily is a limitation to  $1\frac{1}{4}$  cone units, that is, to about 50 minutes of arc. One is now in a position to examine critically the point raised by Dr. Rand, namely my insistence that the geometric image on the retina of the source of light should be as small as possible, in any case not larger than  $\frac{1}{2}$  cone unit. Why, it may be asked, is it necessary to consider the geometric size of the image in view of the fact that its diffraction pattern is so large? The reply is that that geometric size is kept as small as possible in order to concentrate the greater part of the light into the central bright spot and to keep small the physical dimensions of this spot. Thus, a point source having a geometric image on the retina with a diameter equal to  $\frac{1}{10}$  cone unit is found by experiment to have a physiologic diameter of about  $1\frac{1}{4}$  cone units, and another source having a geometric image equal to 1 cone unit is found by experiment to have a physiologic diameter of about 2 cone units. Thus the smaller the geometric diameter, the better. It is for this reason that in my microstimulation apparatus the geometric image is kept small and its size is stated in cone units, so as to guide other research workers who employ this or similar methods.

Dr. Rand points out that my fixation experiments are at variance with the results of Adler and Fliegelman. Such is the case; but (1) my fixation results have been confirmed and extended by Thomson using another method; (2) the unsteadiness found by Adler and Fliegelman may have been a peculiar feature of the single human subject whom

they used for their experiments or may have been due to the method which they employed, which included the use of a flat mirror adhering by surface tension to the curved surface of the sclera; and (3) it is possible that head movements also occurred during the time that the records of ocular movements were being performed. With regard to the last factor mentioned, experiments have recently been performed by Thomson and myself using a method which records eye movements without accompanying head movements. We found astonishing steadiness of the eye during fixation.

Dr. Rand points out that the fixation experiments were performed on only one eye of one observer. This is true. England was engaged in war when these experiments were being performed, and no other subject was found who could spare the time. Only one eye of the subject was used because the other one had inferior visual acuity, which precluded its use for this type of experiment.

With regard to color blindness, Dr. Rand points out that I do not discuss Wright's alternative suggestions for explaining these situations on a trichromatic basis. The reason was that on the whole Dr. Wright's explanations appear to be correct, for many, if not most, color-blind subjects show few if any signs of polychromatic vision. It should be pointed out, however, that, in my opinion, Dr. Wright's explanations of protanomalous trichromatism cannot be regarded as satisfactory, because supporters of the three color theory have given no satisfactory account of the differences in visual perception of normal subjects and of persons with anomalous trichromatism.

Now let us consider hue discrimination. Dr. Rand regrets that I illustrated my arguments with a hue discrimination curve for one subject with normal color vision, "since this curve departs markedly from the careful determinations of other investigators, including the recent work of Wright and Pitt." There seems to be a mistake here. The hue discrimination curves which I considered were those obtained by Steindler, by Jones and by Laurens, and Hamilton. Of Steindler's results, Sir John Parsons stated that, in his opinion, "of these the most accurate and complete are those of Steindler."

In my opinion, Pitt and Wright found hue discrimination inferior to that obtained by the four other investigators mentioned, probably because of the conditions present during their determination. The Wright colorimeter is illuminated by a strip filament tungsten electric lamp, and narrow spectral bands are selected from the spectrum of this source. As a consequence, light intensity is low, and so measurements have to be carried out in a darkened room. The two fields to be compared subtend together about 2 degrees of arc, and they appear to lie on a black background. Thus the observer's eye is in a state of partial dark adaptation, and conditions are not those which usually produce the best hue discrimination. How important may be this use of fully adequate illumination and of a bright surround is clearly seen in the case of high acuity for pattern detail; evidence is now coming to light that these same factors play an important part in achieving the best hue discrimination also.

With regard to the difficulty in explaining the change of hue undergone by colors when their visual angle is reduced or their illumination lowered, Dr. Rand fails to notice the important point, that the change

undergone by color vision when yellow is replaced by white is accompanied with a local fall in the brightness of the spectrum in this region, and that, similarly, the replacement of blue by black is correspondingly accompanied with a localized decrease of brightness, as has recently been demonstrated by Thomson. It is these localized decreases in brightness which accompany the color changes which present to the three color theory so much difficulty. Thus in order to account for the notch in the luminosity curve in the yellow spectral region, discovered by Sloan, the hypothesis was advanced by Forbes that the red receptors retain their sensitivity better than do the green ones or the blue ones. In order to account for the notch in the luminosity curve in the blue spectral region, which has recently been discovered by Thomson, a similar hypothesis must be advanced, namely, that the blue receptors retain their sensitivity better than do the green ones or the red ones. But at the same time that this notch appears, blue is seen to be replaced by dark gray, or even by black, and in order to account for this dramatic color change it is necessary on the basis of the three color theory to assume that the blue receptors are cut off partially or completely from the nerve paths which connect them with the blue-receiving center of the brain. The three color theory is therefore found to be on the horns of a dilemma, because in order to account for Thomson's notch the assumption has to be made that the activity of the blue receptors is enhanced; on the contrary, in order to account for the substitution of dark gray or black for blue, the assumption has to be made that the blue receptors are largely if not entirely, put out of action. But these assumptions are completely at variance with one another, so that either one or the other, but not both, phenomena can be accounted for. To summarize the situation with regard to foveal color vision of test objects which subtend small angles at the eye: In order to account for the observed phenomena on the basis of the three color theory, five supplementary hypotheses must be advanced. Not only do these lend one another no support, but they are not supported by any other evidence. Moreover, two of them are contradictory. Thus the three color theory fails altogether so far as this important phase of color vision is concerned.

This is not an isolated example of the failure of the three color theory to comply with the results of recent research, for an examination of other phases of color vision discloses the fact that it is in no better case with any one of these. The polychromatic theory, on the other hand, has so far been found to be in agreement with them.

Readers of this letter may like to have recent evidence concerning the polychromatic theory. The microstimulation method, which comprised the fixation point method and the subjective color method, provided evidence for the presence of a number of different receptors in the human retina. The approximate wavelengths of the crests of these receptors and the part they play in vision are now known with some degree of certainty.

Three types of receptors play a predominant role in foveal color vision at medium light intensities, and for fields of 2 degrees; these receptors have crests in the spectrum at about 0.60, 0.55 and 0.45 microns. They form together what I have called "the tricolor unit." These are assisted, under the conditions mentioned, by four other types

of receptors, which play a subsidiary part only: a crimson type of receptor, which has responses in the red (0.65 micron) and in the violet (0.42 micron); a yellow type (0.58 micron); a blue-green type (0.50 micron), and a blue type (0.48 micron). When, with foveal vision, the light intensity is slowly increased to a maximum, first the crimson and the blue-green receptors cease to function, and they are followed by the tricolor receptors, so that there is left a form of dichromatic vision mediated by the yellow and the blue receptors only. On the other hand, if light intensity is slowly decreased, it is the yellow and the blue receptors which are the first to go out of action, thus producing the notches in the luminosity curve which are found in the yellow and in the blue. With a further reduction of intensity, the tricolor receptors also lose activity, thus producing another form of dichromatism, for which the crimson and the blue-green receptors are responsible. The replacement of foveal vision by peripheral vision causes changes which resemble those produced by a high intensity of illumination, and a reduction of visual angle imitates the effects of a reduction of light intensity.

The accompanying table summarizes the points which have just been mentioned.

Type of Receptor	Wavelengths (Micron) According to			Foveal Vision				
	Fixating Method	Subjective Method	Other Methods	Very Low	Light Intensity			Very High
					Low	Medium	High	
Red.....	0.66	0.64	0.66	++	+	+	..	..
Orange.....	0.62	0.61	0.60	..	+	++	+	..
Yellow.....	0.58	0.575	0.578	..	..	+	+	++
Green.....	0.54	0.54	0.547	..	+	++	+	..
Blue-green.....	0.50	0.51	0.50	++	+	+	..	..
Blue.....	....	0.48	0.476	..	..	+	+	++
Blue-violet.....	0.46	0.45	0.45	..	+	++	+	..
Violet.....	0.42	0.42	0.42	++	+	+	..	..

Evidence concerning the other methods of investigation, referred to in the table, are in course of publication elsewhere.

H. HARTRIDGE, M.D., London.

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# Abstracts from Current Literature

EDITED BY DR. WILLIAM ZENTMAYER

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## Anatomy and Embryology

NATURE OF THE INNERVATION OF THE CILIARY MUSCLE. P. MATTEUCCI, *Ophthalmologica* 114: 377 (Dec.) 1947.

Histologic studies on human eyes apparently show that both portions of the ciliary muscles (the radial fibers of Brücke and Wallace and the circular fibers of Müller and Rouget) are innervated by parasympathetic and sympathetic fibers. The author was able to demonstrate not only nerve fibers covered by myelin sheaths, but also a network of fine neuro-fibers which end in the neighborhood of the smooth muscle elements.

H. P. KIRBER.

## Conjunctiva

SURGICAL TREATMENT OF PTERYGIA FOLLOWED BY X-RAY THERAPY TO PREVENT RECURRENCE. H. L. HILGARTNER, R. T. WILSON and J. D. WILSON, *Am. J. Ophth.* 31: 667 (June) 1948.

Hilgartner, Wilson and Wilson report gratifying results in 10 cases of pterygium following postoperative irradiation. They describe the roentgenologic technic.

W. S. REESE.

## Cornea and Sclera

ROLE OF VITAMIN INSUFFICIENCY IN THE PATHOLOGY OF THE CORNEA. A. KATZNELSON, *Vestnik oftal.* 26: 3, 1947.

Keratomalacia due to avitaminosis A in the mother is observed in infants, who may be born with dense opacities of the cornea. According to Katznelson's observations, the clinical picture varies in adults and in infants: Avitaminosis A is an early manifestation in infants, while in adults it appears later, possibly because of a reserve of provitamin A in the tissues. The characteristic involvement of the skin and mucous membranes in adults with keratomalacia is less evident in children. Both eyes are usually affected in children, while frequently in adults there is an interval between the involvement of the first and that of the second eye. The secondary purulent infection associated with keratomalacia is less severe in children. The course of the disease in patients with trachomatous pannus is atypical and frequently leads to diagnostic mistakes. In general, the process is more favorable in cases of vascularized corneas. Dystrophy of the cornea occurring in the course of diabetes and toxic diffuse goiter can be explained by endogenous avitaminosis A. The author observed true keratomalacia in a patient with acute hyperthyrotoxicosis. Lagophthalmic keratitis complicating infectious diseases may also be due to endogenous avitami-

sis A. Tuberculous-allergic diseases of the eye are commoner in children with poor nutrition. The cutaneous reaction to tuberculin is also lowered in these children.

The author observed cases of disciform, herpetic keratitis due to thiamine insufficiency. There is a similarity in the clinical picture of neurotrophic and that of neurogenic keratitis of virus origin. The treatment of herpetic keratitis with intravenous injections of thiamine and local application of thiamine ointment gave good results.

Ariboflavinosis causes disturbance of the epithelium of the cornea and increase of the marginal loop vessels, rosacea keratitis and marginal ulcers. Administration of riboflavin is therefore indicated in treatment of these diseases of the cornea. Ascorbic acid is indicated in cases of phlyctens and tuberculous, keratitis and in chemical and thermal burns of the cornea. In the latter, 40 per cent dextrose solution with large doses of ascorbic acid led to a decided lessening of pain, and inflammatory reaction and to decrease in the secondary trophic disturbance of the cornea, with formation of thin scars.

O. SITCHEVSKA.

### General Diseases

THE OCULAR SYNDROME OF CATARACT AND PAPILLEDOMA IN THE MANIFEST FORM OF PARATHYROID DEFICIENCY. D. J. LYLE, *Am. J. Ophth.* 31: 580 (May) 1948.

Lyle reports the case of a woman aged 53 in whom parathyroid deficiency and cataracts developed after thyroidectomy. After cataract extraction of the second eye the patient became confused, disturbed and blind, except for light projection. Papilledema was found, and the fields were greatly constricted. Improvement resulted from use of calcium lactate and dihydrotachysterol.

W. S. REESE.

RUBEOSIS IRIDIS DIABETICA. JACK V. LISMAN, *Am. J. Ophth.* 31: 989 (Aug.) 1948.

Lisman reports a case of rubeosis iridis associated with diabetes in which medical and surgical treatment failed and enucleation was necessary. The eye was examined histologically.

W. S. REESE.

LINDAU'S DISEASE—PROGRESSION IN AFFECTED FAMILY. A. E. MACDONALD, *Brit. J. Ophth.* 32: 575 (Sept.) 1948.

MacDonald had the opportunity to follow the course of Lindau's disease in a family in which 3 of the 4 members of a sibship has each undergone successful removal of a cerebellar tumor, which on pathologic examination proved to be hemangioendothelioma. The diagnosis of cerebellar tumor was verified for sibling 1 at the age of 29 years by pathologic section, and a tumor of the eye was treated by radon seeds. In sibling 2 the cerebellar tumor was diagnosed at operation at the age of 23 years and by pathologic section of material obtained at two subsequent operations. The tumor in the eye presented a similar pathologic appearance. Sibling 3 had a nevus at the limbus of the left eye,

which was less apparent after nine years. The cerebellar tumor of sibling 4, the only male member, was diagnosed by pathologic examination at the age of 28; after extensive irradiation an ophthalmic tumor, of capillary type, has slightly progressed in four years.

W. ZENTMAYER.

OCULAR SYMPTOMS OCCURRING AFTER AMEBIC DYSENTERY AND IN CARRIERS OF THE INFECTION. V. MUCH, *Ophthalmologica* 114: 384 (Dec.) 1947.

Over a number of years, Much collected data on more than 300 patients recovering from amebic dysentery and on carriers of *Endameba histolytica*. He found frequent blepharoconjunctivitis and discoloration of a sector of the temporal half of the optic disk, very similar to that observed in cases of disseminated sclerosis. He found no evidence of iritis. Positive reactions in the complement fixation test and the fluorescein test were accepted as proof of the disease in cases in which organisms were not found in the stool. Much gives 2 Gm. of alkaline fluorescein sodium by mouth and observes a gray discoloration of the aqueous humor under the slit lamp within twenty to thirty minutes in patients with intestinal parasites, liver or gallbladder disease. The same discoloration, however, is observed in cases of pregnancy and hyperthyroidism. In normal subjects a green discoloration appears as a rule in not less than one hour.

H. P. KIRBER.

### Glaucoma

GLAUCOMA ASSOCIATED WITH SUBLUXATION OF THE LENS IN SEVERAL MEMBERS OF A FAMILY. J. P. HARSHMAN, *Am. J. Ophth.* 31: 833 (July) 1948.

Harshman gives the genealogic tree of a family in which there were many cases of glaucoma associated with subluxation of the lens. In these cases the glaucoma was permanently controlled by removal of the lens.

W. S. REESE.

BETA IRRADIATION AS A POSSIBLE THERAPEUTIC AGENT IN GLAUCOMA: AN EXPERIMENTAL STUDY WITH THE REPORT OF A CLINICAL CASE. G. M. HAIK, L. A. BREFFEILH and A. BARBER, *Am. J. Ophth.* 31: 945 (Aug.) 1948.

Haik, Breffeilh and Barber conclude from the results of rabbit experiments that beta irradiation of the ciliary body tends to obliterate the vascular supply and reduce the ocular tension. However, it also causes damage to the lens. A case in which it was tried on a hopeless human eye is presented.

W. S. REESE.

OPERATIVE FAILURES FOR CHRONIC SIMPLE GLAUCOMA: A HISTOLOGIC STUDY. B. F. PAYNE, *Am. J. Ophth.* 31: 965 (Aug.) 1948.

Payne made a laboratory study of cases of operative failures in glaucoma and found in cases of iridectomy that synechias persisted and the root of the iris had not been removed. In iris inclusions there was

closure by the iris and in trephinations fibrotic and inflammatory changes closed the opening. Successful operations far exceed these laboratory "failures."

W. S. REESE.

A MODIFICATION OF ELLIOT'S OPERATION AND ITS APPLICATION TO HIGH TREPHINATION. W. ARKIN, *Am. J. Ophth.* 31:975 (Aug.) 1948.

Arkin modifies the Elliot operation by first making an incision as in cyclodialysis and introducing a spatula, which acts as a support for the trephine and prevents damage to underlying structures.

W. S. REESE.

SOME EXPERIMENTS WITH GREEN SPECTACLES PRESCRIBED TO GLAUCOMATOUS PATIENTS. R. B. ZARETSKAYA, *Am. J. Ophth.* 31:985 (Aug.) 1948.

Zaretskaya finds that wearing green spectacles reduces the tension in glaucomatous eyes and that this effect is reenforced by small doses of epinephrine.

W. S. REESE.

GLAUCOMA AND CATARACT. J. FRANCOIS, *Ann. d'ocul.* 180:457 (Aug.) 1947.

This article is limited to a discussion of the coincidental occurrence of glaucoma and cataract. Cases of cataract secondary to an operation for glaucoma or of glaucoma secondary to a cataract extraction are excluded. The author believes that cases of this nature are frequently overlooked. The presence of a cataract may account for the reduction in vision and obscure a good view of the fundus. The tension should therefore be taken routinely or other confirmatory tests of glaucoma performed if possible.

Cases may be of three types: 1. Chronic glaucoma and the coincident development of cataract. The glaucoma is the more important problem, and the cataract is momentarily of secondary significance. 2. Development of cataract in an eye that had previously been operated on successfully for glaucoma, with formation of a filtering cicatrix. 3. Chronic glaucoma with a high tension which has not been relieved by operation and operable cataract may exist together.

In cases of the first group, if miotics do not successfully control the tension, operation must be resorted to. The iris inclusion operation gives the best results in cases of this type.

In cases of the second category, the surgeon must decide whether he should operate on the cataract, whether he should perform an intracapsular or an extracapsular extraction and what type of operation should be performed so as not to interfere with the filtering cicatrix. The surgeon must be sure of his technic and must be of sufficient character not to hesitate to offer the patient every chance for a successful operation. The author believes that an intracapsular operation should be performed, since an extracapsular extraction predisposes to iridocyclitis and other postoperative complications. The only guide as to when



to operate is the amount of incapacitation produced by the reduction in vision. The type of operation selected should preserve the filtering cicatrix. This is best accomplished by making the corneal incision below and by extracting the lens in the usual manner, but through the inferior incision.

In cases of the last category, the surgeon must decide whether to operate for the glaucoma before or after the cataract extraction or whether to combine the two operations.

A discussion of the various procedures is presented. In the author's opinion an operation for glaucoma, such as iridencleisis, should be performed first. The cataract can be removed later when the eye is quiet.

P. R. McDONALD.

#### VARIATIONS IN GENERAL ARTERIAL PRESSURE AS A CAUSAL FACTOR IN GLAUCOMA. G. CRISTINI, Rassegna ital. d'ottal. 15: 125, 1946.

The author studied the importance of variations in the general circulation as they relate to ocular pressure in glaucoma. He reviews the physiology of the circulation and the neurology of the uvea as these pertain to the hemodynamics of this structure for the regulation of ocular pressure.

He describes the results of three functional tests conducted on 20 glaucomatous patients: (1) inhalation of amyl nitrite with simultaneous recording of the ocular pressure and of the systolic arterial pressure in the arm; (2) phlebotomy and removal of 500 cc. of blood, followed by measurement of the ocular pressure, and (3) consensual response of the ocular tension after compression of the eyeballs.

The difference in the response of the patients to these three tests was noted, a difference which is related to the clinical type of this disease. The author feels that among the causative factors of glaucoma there are not only venous but arterial alterations in the afferent and efferent vessels of the uveal tract. This hypothesis is supported by the response of glaucomatous eyes to various hypotensive substances and is therefore of great importance in the treatment of glaucoma.

G. B. BIETTI—J. J. LO-PRESTI.

#### RETINAL FOLDS AFTER OPERATIONS FOR GLAUCOMA. A. DELLAPORTA, Ophthalmologica 116: 51 (July) 1948.

A case of formation of retinal folds fourteen months after iridencleisis and cyclodialysis for juvenile glaucoma is reported. Retinal folds are not infrequently seen after such operations but are usually due to hypotony of the eyeball. In this case the tension fluctuated between 15 and 22 mm. of mercury. The folds disappeared when the tension rose to 26 mm. and reappeared again with a tension of 17 mm. They persisted for more than two months. They did not cause any metamorphopsia, decrease in visual acuity or changes in the visual fields. The folds were observed with the ophthalmoscope and the slit lamp. An explanation is offered that such folds may be the sequence of a relative hypotony of the eyeball.

H. P. KIRBER.

## Injuries

FURTHER EXPERIENCE WITH AMNIOTIC MEMBRANE GRAFTS IN CAUSTIC BURNS OF THE EYE. A. SORSBY, J. HAYTHORNE and H. REED, *Brit. J. Ophth.* 31:409 (July) 1947.

A further series of 28 cases of caustic burns of the eye treated by grafting with human amniotic membrane is recorded. When the previous and present series are considered together, it appears that remarkably rapid response may be expected when grafting is applied on the same day, or within twenty-four hours after the injury; subsequent recovery is slower. Apparently, the amniotic membrane does not stimulate growth, but acts as a sort of internal splint for the proliferating tissue. The method of preparing the amniotic membrane is described.

W. ZENTMAYER.

## Instruments

OPACITY METER FOR CORNEA AND LENS. H. M. DEKKING, *Ophthalmologica* 115:219 (April) 1948.

The author stresses the need of an objective method for the measuring of changes in density of corneal opacities and cataractous lenses. Repeated determinations of visual acuity are not objective, and slit lamp photography is too expensive. An instrument originally devised by Dekking in 1936 has been improved on (illustration). It consists essentially of a photometer which measures the brightness of an image formed by the anterior segment of the eye.

H. P. KIRBER.

## Lens

CANCER AND THE LENS. E. SACHS and R. L. LARSEN, *J. Ophth.* 31:561 (May) 1948.

Sachs and Larsen discuss factors of biologic, metabolic, physical and chemical nature, any or all of which may be responsible for the immunity of the lens to cancer.

W. S. REESE.

IMPORTANCE OF ZONULOTOMY FOR TOTAL PHACECTOMY (INTRACAPSULAR CATARACT EXTRACTION). L. D'ANDRADE, *Ophthalmologica* 115:78 (Feb.) 1948.

The author has devised a zonulotome which he uses in cases of hypermature, morgagnian and intumescent cataracts and the cataracts of high myopia. After rupturing the lower half of the zonule, he applies pressure to the lowest part of the cornea and effects tumbling of the lens. He uses a special fork-shaped instrument which catches the lens at the limbus and removes it.

H. P. KIRBER.

## Methods of Examination

THE STEREOPHOTOGRAMMETRIC STUDY OF THE ANTERIOR SEGMENT OF THE EYE. E. V. BERTOTTO, *Am. J. Ophth.* 31:573 (May) 1948.

Bertotto describes a new method of obtaining all the curves which make up the anterior segment of the eye based on the application of

stereophotography to ophthalmology. Because of the transparency of the conjunctiva and cornea, he powders the eye with a contrasting medium. The results obtained were better than were expected, the margin of error being only 0.017 mm. This method should be of great value in the manufacture of contact lenses.

W. S. REESE.

### Neurology

WARREN TAY-SACHS DISEASE IN A CHINESE INFANT. G. HARIDAS, Brit. J. Ophth. 31:428 (July) 1947.

A case of amaurotic family idiocy occurring in a Chinese Hylam male infant is reported, the first of its kind from Malaya. The child was 20 months and 20 days old when he died. The diagnosis was based on the progressive muscular weakness, lack of mental development and blindness, with pathognomonic changes in the fundus.

The article is illustrated.

W. ZENTMAYER.

### Ocular Muscles

NOTE ON THE POSITION OF THE EYE IN A THIRD NERVE PALSY. E. WOLFF and HEFFERNAN, Brit. J. Ophth. 31:427 (July) 1947.

A photograph of a patient is shown to demonstrate that with complete third nerve palsy the eye is abducted but, as in this position the superior oblique muscle cannot depress the eye, or only slightly, the amount of depression is minimal or nil. In the case reported, the paralysis was in the left eye, and when the lid was lifted manually the eye was seen to be directed directly outward. The corneal images were on the same horizontal level.

W. ZENTMAYER.

### Operations

SOME NEW POINTS IN THE TECHNIC OF IMPLANT IN TENON'S CAPSULE AFTER ENUCLEATION. A. FAVORY, Brit. J. Ophth. 32:366 (June) 1948.

Favory is of the opinion that an implant of 10 mm. in diameter is sufficient. Acrylic resin is the material used. The implant is spherical and slightly flattened posteriorly. Four small arches made of acrylic resin are fixed near the anterior surface to receive the tendons of the rectus muscles. On the anterior aspect a spur 15 mm. long and quadrangularly prismatic is drawn out. On the implant body are four grooves for easing the muscle looping. At the end of the operation only the spur protrudes from the conjunctival covering; the spur later fits into a hole on the posterior surface of the prosthesis. Silk sutures are used.

The necessary cuts for an understanding of the technic are supplied.

W. ZENTMAYER.

A NEW OPERATION FOR IRIDODIALYSIS BY MEANS OF AN IRIS SUTURE. A. GARDILČIĆ, Ophthalmologica 115:141 (March) 1948.

Two cases of traumatic iridodialysis are reported in which the author used a corneoscleral surgical suture which unites the lips of the

wound after keratome incision, catches the root of the iris and emerges subconjunctivally under a Kuhnt-Pflüger flap. H. P. KIRBER.

### Orbit, Eyeball and Accessory Sinuses

MICROPHTHALMOS. G. FORBES, Brit. J. Ophth. 30:709 (Dec.) 1946.

In the case reported the clinical diagnosis was bilateral microphthalmos, but, as in many such cases, histologic examination demonstrated the presence of a cyst attached to the lower anterior part of the eye. A female infant was born after completing the sixth month of intra-uterine life, but before reaching the seventh month. The infant lived thirty hours. Besides the ocular abnormalities, there were supernumerary digits on the ulnar side of the right hand. The cyst was not completely cut off from the cavity of the eye, and fragments of disorganized retinal tissue passed through the gap. The interior of the cyst contained a mass of plicated, disorganized retina, being opposed to the choroid in some places and to the fibrous wall of the cyst in others, and also apparently lying free in the cystic cavity. The outer wall of the cyst was continuous with the sclera and appears to be of the same consistency, and in other places it was much less dense. This finding suggests that the wall was imperfect and had been reenforced by condensed orbital fibrous tissue. The article is illustrated.

W. ZENTMAYER.

EXPULSIVE HEMORRHAGE: TWO REMARKABLE ANATOMIC DISCOVERIES. W. A. MANSCHOT, Acta ophth. 19:237, 1941.

The author examined 2 globes, in each of which an expulsive hemorrhage had occurred. In 1 eye there was observed an angioma arising from one of the branches of a vortex vein. In the other eye there were areas of necrosis in the ciliary arteries, together with thrombus formation. The author believes that the vascular necrosis was the result of glaucoma, with which the eye had been affected for many years.

O. P. PERKINS.

### Physiology

ON OBJECTIVE ADAPTOMETRY. G. H. JONKERS, Ophthalmologica 114:397 (Dec.) 1947.

The method first devised by Rieken (1943) was improved on by the author, who measures optokinetic nystagmus in dark adaptation by means of an improved adaptometer, a cathode ray oscillograph and a string galvanometer for registering the movements of the eye. He was able to measure objectively a  $10^6$ -fold increasing sensitivity.

H. P. KIRBER.

STEREOSCOPIC VISION IN LIGHT AND DARK ADAPTATION. A. GUGGENBUHL, Ophthalmologica 115:193 (April) 1948.

Central and peripheral stereoscopic vision were determined in light and dark adaptation by means of an apparatus originally described by

Monje. For central vision in dark adaptation the threshold was found to be three times as high and the threshold for peripheral vision 1.7 times as high as that in light adaptation. Findings of earlier investigators were confirmed in general, and the differences were explained by comparing the different technics. The fact that the threshold of peripheral vision increases threefold in daylight and hardly changes in dark adaptation proves that stereoscopic vision of the dark-adapted eye is a function of the paracentral parts of the retina. Stereoscopic vision decreases toward the periphery of the retina in the same manner as does the visual acuity.

H. P. KIRBER.

### Retina and Optic Nerve

FAT EMBOLIZATION INVOLVING THE HUMAN EYE. M. H. FRITZ and M. J. HOGAN, *Am. J. Ophth.* 31: 527 (May) 1948.

Fritz and Hogan discuss the etiology and mechanism of the production of fat emboli. They report a case in detail, describing the clinical and pathologic findings. The fundi showed round and oval, white sub-retinal exudates completely surrounding both maculas and following the course of the main retinal vessels. The macula in the right eye appeared cherry red. There were no hemorrhages. W. S. REESE.

CAPILLARY HEMORRHAGES OF THE RETINA AND CAPILLARY FRAGILITY. J. GOEDBLOED, *Ophthalmologica* 115: 174 (March) 1948.

Common causes of capillary hemorrhages are trauma, toxic and inflammatory processes, blood dyscrasias, arteriosclerosis, hypertension and diabetes. The Göthlin index is best suited to the measurement of capillary fragility. The American literature on butin is reviewed in part, and 2 cases are reported in which the condition was successfully treated with this drug.

H. P. KIRBER.

### Uvea

CUTANEOUS ALLERGY TO TUBERCULIN IN IRIDOCYCLITIS. M. DUBOIS-POULSEN and DUBOIS-VERLIERE, *Ann. d'ocul.* 181: 65 (Feb.) 1948.

Investigation on cutaneous allergy in cases of tuberculous uveitis has been generally neglected. The frequent positive cutaneous reactions in adults makes it difficult to determine whether or not the lesion actually is tuberculous. The French school does not agree with the German that in the majority of the cases uveitis is due to tuberculosis. Lagrange stated the belief that only a negative cutaneous reaction is of value. The authors believe that this subject deserves more accurate evaluation and that a more critical quantitative method of testing should be used. The merits of the Pirquet cutaneous inoculation and of the Mantoux intradermal injection of tuberculin are discussed.

In the authors' investigations the intradermal test was used. Injections of 0.1 cc. of old tuberculin in dilutions of 0.001, 0.0001, 0.00001 and 0.000001 mg. per cubic centimeter were given intradermally. The

solutions were freshly prepared each time that they were used. All four injections were made at the same sitting. The cutaneous reaction was noted in twenty-four hours. A reaction was considered positive if the area of reaction to the two weakest dilutions was 4 mm., or 10 mm. in diameter to the two stronger dilutions. The reactions were graded as negative, weak, moderate or strong, the last constituting a definite reaction to the two weakest dilutions.

Of 55 cases of uveitis, a strong reaction was noticed in 62 per cent. Of the same group, the uveitis was believed to be due to other etiologic factors in 15 cases; in 47 per cent of which the Mantoux test was positive. Of 73 cases in which the condition was judged to be tuberculous from the clinical findings, the reaction was positive in 84 per cent.

The authors conclude with an interpretation of the positive and negative results.

P. R. McDONALD.

# Society Transactions

EDITED BY DR. W. L. BENEDICT

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COLLEGE OF PHYSICIANS OF PHILADELPHIA, SECTION ON OPHTHALMOLOGY

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*April 24, 1947*

**Rubeosis Iridis Diabetica: Report of a Case.** DR. JOSEPH WALDMAN  
and (by invitation) DR. DAVID NAIDOFF.

Rubeosis iridis is a comparatively rare condition in which a non-inflammatory proliferation of new blood vessels occurs on the anterior surface of the iris and which is usually associated with glaucoma. Salus, who first described the condition in 1928, used the term rubeosis iridis diabetica when he observed it bilaterally in 3 cases of diabetes, in all of which glaucoma eventually developed.

The appearance of the iris is characteristic; the anterior surface is covered with radially arranged new vessels, especially near the sphincter region, where the individual vessels anastomose to give the appearance of a ring about the pupil. The vessels end at the pigmented margin, without extending over it. Beginning at this capillary net, larger vessels spread over the iris and disappear in the angle of the anterior chamber. In 1937 Kurz first described the gonioscopic and pathologic features. Gonioscopic study revealed large vessels running peripherally into the angle, where they divided into innumerable branches to connect directly with Schlemm's canal and to form extensive peripheral synechias. With the development of atrophy of the iris the vascular net in the rubeotic eye tended to disappear. Pathologic study revealed that the new vessels were unassociated with inflammation or with newly formed tissue but lay in and on the iris itself. Hemorrhagic retinopathy and a tendency to vascular proliferations in and on the retina and the optic nerve was a frequent concomitant change.

Hyphema was common, and in all reported cases a recalcitrant glaucoma resulted, which yielded only temporarily, or not at all, to treatment, either medical or surgical. In 1940 Fralick reviewed 32 reported cases of rubeosis iridis associated with diabetes and added 3 cases which he had observed; in only 1 of the 35 cases did glaucoma fail to develop, and in this case, reported by Wegner in 1939, treatment was considered successful when an intracapsular cataract extraction was performed. Since then, Meyer and Steinberg, Scobee, Grury and deRoeth have reported the use of cyclodiathermy in controlling the glaucoma in rubeosis iridis diabetica, although this treatment resulted in atrophic eyes.

An interesting observation is the relation of arterial hypertension to rubeosis; this was first mentioned by Kurz. Fralick, in his review, found hypertension in 16 of the 35 cases. It seems that diabetes and

hypertension together in the same patient are associated with a much higher percentage of vascular pathologic change than when either is present alone.

The following case is from the No. 2 ophthalmologic service of the Jefferson Medical College Hospital.

M. G., a woman aged 58, first learned in 1943 that she had diabetes. Subsequent treatment had been dietary and haphazard. Insulin had not been used. For the six months prior to admission she had also been treated for hypertension. In December 1946 she had suffered sudden loss of vision in her left eye, which was said to be due to a severe hemorrhage in the vitreous. On Feb. 24, 1947, one week before her admission to the hospital, the patient became aware of what she termed "pink vision" in her right (good) eye; everything at which she looked had a reddish hue. That night she had severe pain in the right eye, and the next morning vision was limited to light perception. That day she was seen by one of the members of the staff and a diagnosis of acute glaucoma was made. At this time hyphema was present. Treatment consisted of administration of physostigmine in drops and application of hot compresses, but the elevated intraocular tension, pain and loss of vision persisted until her admission to the hospital, on March 1.

On her admission, ophthalmologic examination revealed that vision was limited to light perception in the right eye and was 4/60 in the left eye. Intraocular pressure (Schiotz) was 65 mm. in the right eye and 16 mm. in the left eye. The right eye was severely congested throughout. Biomicroscopic examination showed that the cornea was edematous; many small, gray, keratic precipitates were present. The aqueous was slightly turbid. The stroma of the iris was atrophied, and a narrow ectropion uvea extended around the entire inner border of the pupil. Just outside this pigmented margin of the pupil was a fine network of new-formed blood vessels, which covered the sphincter zone in a wreathlike fashion and gave a reddish hue to this portion of the iris. From this vascular zone on the surface of the iris several more or less straight, and larger, vessels coursed toward the base of the iris; some terminated in tufts of small capillary networks at about the base of the iris; others disappeared behind the limbus. Uveal pigment and grayish debris were noted on the anterior surface of the lens, which had undergone general loss of transparency with other cataractous changes. Examination of the fundus was impossible because of the changes in the media.

Externally, the left eye presented a normal appearance. The vitreous was loaded with fine and coarse opacities. Many infiltrates typical of diabetes were noted in and about the macular area, and numerous retinal hemorrhages, both punctate and flame shaped, were present throughout. The retinal arterioles showed advanced sclerosis. Biomicroscopic examination revealed numerous fine gray and brown keratic precipitates. The anterior chamber was clear. Atrophy of the iris stroma and absorption of iris pigment were evident. On the iris, near the pupillary border, at about 9 o'clock, a tiny network of new vessels was noted. The changes in the lens were similar to those seen in the right eye.

General physical examination showed a blood pressure of 210 systolic and 120 diastolic, generalized arteriosclerosis and slight cardiac enlargement.



The Kahn reaction of the blood was negative. The blood sugar measured 235 mg.; the blood urea nitrogen, 25 mg., and the serum cholesterol, 222 mg., per hundred cubic centimeters. Urea clearance was 35 per cent. Coagulation time was three and one-half minutes; bleeding time was one and one-quarter minutes; capillary fragility (tourniquet test) was normal. The urine showed 4 plus reaction for albumin, a trace of sugar and many red blood cells and epithelial casts.

The electrocardiogram showed slight left axis deviation; there were no other findings indicative of myocardial change.

The diagnosis was rubeosis iridis diabetica and secondary glaucoma in the right eye and diabetic retinopathy and retinal arteriosclerosis in the left eye; diabetes mellitus; arteriosclerotic and hypertensive renal disease, and generalized arteriosclerosis.

As miotics, physostigmine, neostigmine, and DFP (di-isopropyl-fluorophosphate) were all employed, without any decrease in the intraocular tension; on the contrary, these drugs increased the pain and caused incessant vomiting, which prevented proper control of the diabetes. Pilocarpine nitrate, 8 per cent, was then used, with similar results, even when the strength was reduced to 1 per cent. After three weeks, since no beneficial results were obtained, all miotics were discontinued, and the patient became fairly comfortable, although vision was completely lost. From the time of her admission the patient had received 20 mg. of rutin four times a day. On April 4, 1947, the patient again suddenly experienced excruciating pain in the right eye. Examination then revealed a severe hyphema with intraocular pressure of 68 mm. of mercury (Schiotz). The pain has now diminished, but the hemorrhage in the anterior chamber is still present. The patient's family was informed that operative procedures were usually unsatisfactory in these cases and that enucleation was to be considered for the relief of intractable pain.

#### DISCUSSION

DR. BURTON CHANCE: I recall a case of rubeosis in the service of the late Dr. Schwenk, twenty or more years ago, in a diabetic woman, who failed to return for further study because, so we were informed, she died of her general disease. I have not seen another case since.

**Contaminated Ophthalmic Ointments.** DR. LOUIS LEHRFELD and DR. EDWARD J. DONNELLY.

This paper was published with the discussion in the July 1948 issue of the ARCHIVES, page 39.

**Infections of the Vitreous and Streptomycin: Experimental Studies.** DR. IRVING H. LEOPOLD and (by invitation) DR. RICHARD DENNIS and MARJORIE WILEY, B.A.

Streptomycin penetrates poorly from the blood stream into the vitreous humor of normal rabbit eyes. Local methods of administering the drug were studied and compared for their abilities to produce adequate concentrations of streptomycin in the vitreous. Subconjunctival injections, injections into the anterior chamber, and retrobulbar injection of streptomycin with iontophoresis in the anterior

segment produced higher levels than those obtained with systemic administration. These methods were tried against the standard infections of the vitreous produced by colon bacteria. Direct intravitreal injection of streptomycin, retrobulbar injection with iontophoresis and injections into the anterior chamber reduced the severity of experimental infections of the vitreous due to colon bacteria. They were effective in the order listed. Direct intravitreal injections of streptomycin produced retinochoroidal exudation and subsequent degeneration. In concentrations below 800 micrograms per injection, the damage was minimal and was limited to the site of injection.

DR. RICHARD DENNIS: From the work that we have done, it seems that direct intravitreal injection is the most efficacious of the local methods of administering streptomycin. It also appears that the injection of reasonable quantities of streptomycin, at least up to 800 micrograms, can be made with no more damage than would follow a similar direct injection of saline solution. With improved methods in the refinement of production of the drug this relative safety will probably be more obvious. In the case of a severely infected eye, in which other remedies have proved to be of no avail, the ophthalmologist would seem justified in trying this method. For intravitreal injections the solution should be as near isotonic as possible. In the lower concentrations this isotonicity is best obtained by diluting the drug in isotonic sodium chloride solution U. S. P. In higher concentrations considerable osmotic effect occurs, and here it is best to dilute with distilled water.

DR. IRVING H. LEOPOLD: For the benefit of those who might try retrobulbar injections of streptomycin, it is necessary to point out that such injections may be painful. Intramuscular injections of streptomycin are painful to some persons. Procaine does not interfere with the action of streptomycin and could be used with, or prior to, retrobulbar injections of streptomycin.

### Role of the Vertically Acting Muscles in Concomitant Strabismus.

DR. EDMUND B. SPAETH.

A series of cases was presented to illustrate the role which the vertically acting muscles must play in the causation of convergent, as well as divergent, strabismus. The cases illustrated a relation of the conjugate muscles to muscle overaction in one eye and to muscle underaction in the other eye, a degree of vertical deviation being always present but changing with each possible position of the lateral rotations. Further, overaction was found to be fairly common in the homolateral antagonistic muscles with and without disturbances of the contralateral conjugate muscles. The various possible combinations were presented.

Disturbances in the vertically acting muscles modify to a high degree the corrective surgical measures necessary. Certain rules with respect to the sequence of the necessary operations (lateral and/or vertical) in the various situations seen were presented.

### DISCUSSION

DR. GLEN G. GIBSON: Once again, we are indebted to Dr. Spaeth for calling out attention to an extremely important, and frequently neglected, phase of ophthalmology. The time has come when we can

no longer neglect the subject of the role of the vertically acting muscles in horizontal strabismus. This is an important paper, for two reasons: (1) It brings us intimately into contact with Dr. Spaeth's extensive surgical experience in these complex cases. (2) The literature in the past has been inadequate as a guide to the handling of such cases; yet it illustrates the fact that we as clinicians are in need of precise definitions by which we can understand each other more thoroughly when we use such terms as spasm, overaction, vertical component and vertical element.

This paper is too all inclusive and extensive for one to discuss all the aspects of it, and I feel that I may best serve our purpose by summarizing briefly what Dr. Spaeth has said. He has pointed out that there are cases of pure horizontal deviation without any vertical element. He has also pointed out that if one studies such cases carefully one can determine in many of them that there is vertical imbalance, either hypertropia or hyperphoria. The careful study of these cases is rewarded by a much better surgical result. There are two main groups in which combined vertical and horizontal tropias are encountered. The first type is primarily a concomitant strabismus with a secondary vertical deviation. The commonest of these is the type in which there is bilateral overaction of the inferior oblique muscle. The overaction of the inferior oblique is merely the secondary participation of these muscles in the esotropia. The second type is of primary paralytic origin and the vertical deviations are primary, the horizontal deviation being merely the secondary device that the patient uses to avoid the disturbing diplopia which results in cases of vertical deviation. The differential diagnosis of these two types is relatively easy when one considers that when the horizontal deviation is primary the excessive action of the inferior oblique muscle is bilateral. It is equal and symmetric. In other words, both inferior oblique muscles participate equally. It is just the reverse in the cases in which the vertical deviation is primarily paralytic in origin; then the deviation is always different in the two eyes. The deviations are not symmetric, and the difference between primary and secondary deviations can usually be measured.

There is a third type of mixed deviation in which the eyes have become so concomitant that it is impossible to tell precisely which muscle was primarily involved. Some ophthalmologists will not admit that in cases of deviations which were originally paralytic the eyes become progressively more concomitant as time passes, so that it is impossible to identify the original offending muscle; I feel, however, that such cases occur frequently.

Dr. Spaeth has called attention to the vital importance of sensory correspondence in these cases. I should like to cite 2 cases, both of men aged 22, which illustrate this all-important point. Both patients had 10  $\Delta$  of left hyperphoria when measured in the primary position. The first man presumably had had normal eyes and normal binocular vision up to the time of an automobile accident, at the age of 22, when a typical paresis of the left superior oblique developed. A complete myotomy was performed on the inferior oblique muscle of the offending eye, with the resultant reduction of hyperphoria to 0.5  $\Delta$ . This excellent result is due to the normal binocular sensory correspondence before the onset of the condition.

The other man had an entirely different history, and a much greater surgical correction was necessary. This condition was also a paresis of the superior oblique muscles, onset of which was at 2 years of age; the patient had very abnormal sensory correspondence and the surgeon could get little help from the binocular reflexes in maintaining alinement. Even the deviation was essentially difficult to determine, as was the diagnosis, in view of the extremely abnormal sensory correspondence. Myotomy of the inferior oblique muscle on the offending side was combined with a 3 mm. recession of the contralateral inferior rectus muscle. The residual hyperphoria was 3  $\Delta$ , even though the correction had been more extensive. It is important to know the status of the sensory mechanism before attempting surgical correction in cases of vertical deviation.

Dr. Spaeth has called attention to the importance of recognizing inhibitional palsy in cases of these deviations. I would refer you to an article by Dr. F. H. Adler (*Tr. Am. Ophth. Soc.* 81: 255, 1945) which is clear on this subject. The problem has also been discussed, though less clearly, by Chavasse (*Worth's Squint*, Seventh Edition by F. Bernard Chavasse, Philadelphia, P. Blakiston's Son & Co., Inc., 1939). Dr. Spaeth has called attention to the fact that more than a cosmetic result is desired, and that the obtaining of binocular vision may be the ideal sought.

The most important factor in obtaining binocular vision in these cases is the age at which surgical treatment is instituted. It is not necessary to operate before the patient is 3 years of age, nor desirable to delay until the child is past 4 years old. In other words, the ideal time for surgical correction is between 3 and 4 years of age. If the child is treated at that age, he is still immature enough to acquire normal binocular vision. Dr. Spaeth has pointed out that with disturbances of the vertical muscles associated with horizontal deviation the results are frequently better than with the purely horizontal deviations; it has been my experience that the results of surgical correction of the vertical muscles, when the condition has been correctly diagnosed and proper treatment carried out, has been more satisfactory than the results which have been achieved in the uncomplicated cases of horizontal deviation.

DR. GEORGE F. J. KELLY: I should like to ask Dr. Spaeth what his experience has been in cases of torticollis due to paralysis of an oblique muscle. When does the torticollis disappear after correction of the defect of the oblique muscle?

I think Dr. Spaeth stated that when there are both a vertical and a lateral component he operates first on the muscle with greater paralysis. I also understood him to say that with correction of the horizontal component there is always improvement in the vertical component and that with correction of the vertical component there may be no alteration in the horizontal component. Would it not be worth while to operate on the horizontal component? One would surely get some correction of the vertical component, and perhaps one would not later have to do so much on this component.

DR. EDMUND B. SPAETH: Dr. Gibson brought out three points which are quite true. The first was stated by Dr. White on this floor

many years ago, "Seventy-five per cent of concomitant strabismus is accompanied by a vertical deviation"; too often, nothing is done about it.

Dr. Gibson spoke of "so many millimeters of recession or resection." Many things enter into the surgical correction of a vertical deviation. To correct such a deviation by millimeters is quite impossible. It is disheartening to see the poor results one obtains in any type of operation on an inferior oblique muscle when, instead of operating on an inferior oblique muscle, one should have made the opposite surgical correction, that is, resection or recession of the superior oblique muscle. It is only by comparison of the total amplitude of the action of the conjugate yoke muscle with that of the muscle involved that one can decide whether an inferior oblique or a superior oblique muscle should have been operated on.

As to torticollis, there is no question about this except concerning the time of its disappearance. If torticollis is not improved by monocular occlusion, prior to operation, it will take a long time to disappear.

As to the sequence of surgical procedures on the vertical and the lateral components, I have been distressed and embarrassed several times to find that subsequent correction of the vertical muscles has upset the previous surgical result on the lateral muscles. If the vertical component of the deviation is the greater, it is wise to take care of that before correction of the lateral deviation is even attempted, for one cannot tell for certain the effect on the lateral deviation.

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#### NEW YORK ACADEMY OF MEDICINE, SECTION OF OPHTHALMOLOGY

W. Guernsey Frey, M.D., *Chairman*

Maynard C. Wheeler, M.D., *Secretary*

Oct. 20, 1947

#### INSTRUCTION HOUR

**The Surgical Technic of and Indications and Contraindications for Keratoplasty.** DR. R. TOWNLEY PATON.

#### REPORT OF CASES

**Scleromalacia Perforans.** DR. MELVIN HARBATER (by invitation).

The disease is probably a manifestation of the rheumatoid diathesis and is characterized by the appearance in the sclera, anterior to the equator, of small yellow excrescences, which break down, producing holes in the sclera and exposure of the underlying uvea. The early lesion is a small sterile abscess. With extension of necrosis and sequestration of scleral tissue, the characteristic hole is produced. The pathologic picture is essentially that of rheumatoid disease in any connective tissue. Visual disturbances and other symptoms are produced by complicating disease, especially uveitis.

A characteristic case was presented.

## DISCUSSION

DR. EDWARD DOUGLAS (by invitation): I have seen 2 other cases of scleromalacia perforans; in both the condition was associated with rheumatoid arthritis, and the patients were characteristically malnourished and asthenic. That rheumatoid arthritis is of infectious origin and usually occurs at a much earlier age suggests the possibility that it is an earlier stage of the same pathologic process as scleromalacia. Could it be a degenerative process superimposed on the rheumatoid disease?

Zinc oxide (20 per cent) administered locally has been suggested in treatment of this condition. It is doubtful whether this medication will help to repair a hole. Vail has proposed scleral resection to repair the hole. The multiplicity of holes makes this of questionable value.

The pathologic process is slowly progressive and eventually leads to destruction of the eyeball. In the case presented it will be of interest to see whether the process will advance beyond the equator.

DR. MELVIN HARBATER: I believe that zinc oxide was used in 1 of the doubtful cases of scleromalacia. I doubt whether it has any effect on the disease.

## PAPERS OF THE EVENING

**Changes in the Fundus in Young Veterans.** DR. SANFORD R. BLOOMENTHAL (by invitation).

Four cases of lesions of the fundus in young veterans representing chorioretinitis of probable tuberculous origin; atrophy of the optic nerve without changes in the field; retinal hemorrhages accompanying purulent dermatitis; retinitis proliferans with detached retina, respectively, were presented.

## DISCUSSION

DR. BRITAIN F. PAYNE: One is at a loss to know the cause of many such lesions of the fundus. The effect of Army rations, or lack of rations, of exposure to heat and cold and of various diseases and injuries is portrayed in the cases just presented. "Trench foot" and cardiovascular and nephritic disease were common in these patients.

I have a few lesions to add to Dr. Bloomenthal's list: hole in the macular region, block of the inferior temporal artery and retained foreign body.

**Postvaccinial Ocular Syndrome.** DR. EMANUEL ROSEN, Newark, N. J. (by invitation).

Two types of ocular complications follow vaccination: (a) pustule formation, following accidental inoculation, and (b) ocular complications following or associated with the systemic response to vaccination. Of the first variety several hundred cases have been reported; of the second there are only a dozen recorded in the world's literature. An attempt was made to show that the pathologic process in postvaccinial encephalitis and the process in the other virus exanthems are identical and that the ocular syndrome is of necessity related to, and a part of, the encephalitic picture.

Several cases of ocular complications were described, including interstitial and dendritic keratitis, choroiditis, iritis, thrombophlebitis, central serous retinopathy, thrombosis of the central retinal vein, thrombosis of the central retinal artery and panophthalmitis. These complications all occurred ten to twenty days after vaccination.

**Mild Glaucoma.** DR. ADOLPH POSNER and DR. ABRAHAM SCHLOSSMAN (by invitation).

In 40 of a series of 373 cases of primary glaucoma the disease remained unusually mild throughout the entire course. Several of the patients were observed for many years. In some cases the condition was discovered accidentally during routine examination; in others the diagnosis was made because of the presence of glaucoma in other members of the family, while in still others mild symptoms of glaucoma were complained of. In such cases the ocular hypertension is not very high and is generally well tolerated. A good response to miotic therapy is the rule. The visual fields show no deterioration during the entire period of observation, and the fundi and visual acuity remain normal. Cases in which the elevation of tension was the only sign of glaucoma were included if a provocative test or a pupillographic examination or both gave a positive result. Three case histories were presented.

#### DISCUSSION

DR. OTTO LOEWENSTEIN (by invitation): There are two points I wish to stress: (1) pupillography as applied to glaucoma and (2) the question of heredity.

Pupillography had proved to give clinical access to the autonomic centers, and therefore I was very much interested in doing work on glaucoma, for the development of which central nervous factors were frequently considered, but had never been shown, to be responsible. I made examinations in cases of both early and more advanced glaucoma and found that symptoms of central autonomic origin existed to an equal degree in the two types. Sometimes, they were even more pronounced in early than in advanced cases. The pupillographic pictures showed certain characteristics of the central autonomic nervous system which were different from those of other well known types of central lesions. They were always present on both sides, even in cases in which clinically the condition was unilateral. These facts, in connection with the peculiarities of the pupillographic findings, pointed to the posterior part of the hypothalamus as a possible site of the lesion.

The number of patients, about 70, examined pupillographically is too small for general conclusions. At this stage of development of the problem the contributions which I am able to make to the clinical diagnosis of glaucoma in initial and doubtful cases may be cautiously defined as follows: There is a connection, causal or not, between hypothalamic lesions and simple glaucoma. When in a clinically doubtful case the characteristic pupillographic symptoms cannot be detected, the condition is likely to differ from glaucoma. Where they are detectable, glaucoma is possible, though not proved.

This brings me to the second point, that of heredity. In the small space of the hypothalamus, a great number of vegetative centers have

been localized which under pathologic conditions may produce very different syndromes, such as hypertensive vascular disease, diabetes insipidus, diabetes mellitus, exophthalmos and, briefly, all those conditions dependent on the hypophysiodiencephalic system. Either they, or glaucoma, or even both, independently or jointly, may appear as neighborhood symptoms. It would be difficult to understand that the hereditary disposition to disease processes within this small area would be a selective one in the extreme sense that it might be concerned with individual nuclei, and not with the area as a whole. This is the theoretic reason that I feel that studies in the genetics of glaucoma should include all possible disorders of the interbrain, and it is for this reason that I agree completely with the approach to the problems of glaucoma shown so ably by the speakers.

Let me finish by emphasizing that all this work is still in its beginning; but it is a promising beginning.

DR. SYLVAN BLOOMFIELD (by invitation): It may be of interest to mention a case in the glaucoma clinic at the New York Eye and Ear Infirmary. It emphasizes the point these authors have made concerning the unpredictability of the course that mild chronic simple glaucoma may take.

A white woman aged 48 had been followed in the clinic since 1931. At that time a diagnosis of bilateral chronic simple glaucoma was made and amply confirmed by the subsequent course. Between 1931 and 1942 she presented a tension of 35 mm. in both eyes on numerous occasions, and at one time a tension of 45 mm. was noted, in spite of the regular use of pilocarpine. For a brief period physostigmine was employed to keep the tension within normal limits. Because of elevated intraocular pressure, in spite of miotic therapy on two occasions, surgical intervention was advised but was refused. At no time was evidence of intraocular inflammation or acute congestion noted.

In 1942, because of persistently normal tension, use of miotics was discontinued, and no medication has since been employed. She has been seen regularly in the clinic, and at no time in these past five years has she shown a tension of over 26 mm. Vision in each eye is correctible to 20/25, and her fields are normal except for slight enlargement of both blindspots, a sign not particularly characteristic of glaucoma. She has been asked to enter the hospital for further study but has refused. A lability test made recently showed a result for both eyes that was within the upper range of normal. Clinically this patient has presented no evidence of glaucoma for five years. However, there seems no doubt of the diagnosis, and I present her case as an example of an unusually prolonged and fairly complete remission.

DR. ABRAHAM SCHLOSSMAN: Dr. Bloomfield's case is enlightening. I saw the patient with him this afternoon. If the tension is found to be elevated, no other signs of glaucoma are present and the fields are normal, one can delay treatment. The physician should keep the patient under observation for a few months before beginning treatment with pilocarpine and make certain of the diagnosis before starting the use of miotics. Many patients associate glaucoma with blindness, and it is important for the ophthalmologist to treat the patient psychologically. A note of optimism expressed by the physician may in itself contribute to keeping the disease in check.



## A Procedure to Make the Elliott Trephine Operation Less Difficult.

DR. RAYMOND E. MEEK.

A simple method of performing the Elliot corneoscleral trephination was presented. Benedict's method of making the conjunctival flap so as to include Tenon's capsule was used. With a Wheeler or a Lunsgaard knife, an incision is made at the corneoscleral junction through one-half the thickness of the margin. The knife blade must be held perpendicular to the eye. The cornea is now easily split to a distance of 1 mm. With the trephine placed astride the corneoscleral margin and with the lower raised portion with its attached conjunctiva used as a stop or shelf, the opening is made. The trephine should be held perpendicular in order to get a cleancut disk or plug. The tissue of the iris, which now presents, is grasped near its base with iris forceps. With slight tension pulling the iris toward the pupil, the tissue is excised. If no prolapse of the iris occurs, it may be withdrawn by suction. The conjunctiva-Tenon capsule flap is replaced and sutured. Gentle massage is begun on the third day and kept up daily until the wound is healed and the circulation of aqueous established. A dressing is kept on the eye for a week.

### DISCUSSION

DR. WILLIS S. KNIGHTON: I am in general accord with Dr. Meek's presentation of the operative procedure, but a few points merit discussion.

First, I do not agree with the practice of doing a paracentesis in the morning to lower the tension for an operation in the afternoon. It has been my experience that such paracentesis wounds have to be reopened two or three times a day in order to keep the tension down. If a paracentesis were done in the morning on an eye with a tension of 40 mm., I should expect to find the tension up to 50 mm. or more within a few hours, as the result of the secondary aqueous. It is better to reduce the initial tension by means of retrobulbar injection or by intravenous injection of dextrose solution. If these measures fail, one can then resort to posterior sclerotomy.

The question of late infection following trephination has little to do with the technic of the operation itself. One might almost say that the infection is a matter of luck; if the patient has a clean conjunctival sac, the eye will not become infected, but in the presence of conjunctivitis his eye is more liable to infection because of the thin bleb.

The preparation of the conjunctival flap is important; like Dr. Meek, I have had best results by following Benedict's technic. It is also well to dissect as little as possible in a horizontal direction in order to preserve untraumatized tissue at the sides of the trephine opening.

The technic of splitting the cornea is one that must be learned by experience. Many operators start this procedure with a sharp instrument and then change to a blunt dissector. Others feel that any blunt dissection is uncertain, or even dangerous, and prefer to complete splitting the cornea with a sharp instrument. My own preference is for the sharp dissection because I feel greater security in doing it that way. I do not know whether Dr. Meek's suggestion of first splitting the tissue vertically would simplify matters or not; perhaps he found it easier only because he has had considerable experience in the operation.

The necessity of splitting the cornea is evident when one refers to the measurements within the eye. According to Salzmann and others, the limbus is a zone about 1 mm. wide just peripheral to the end of Bowman's membrane. In practice, however, one looks for "clear cornea" as the dividing line when splitting the cornea. Dr. Johnson has made the interesting observation that the appearance of clear cornea cannot exist beyond Descemet's membrane; even though the outer layers of the cornea are clear, the inner layer cannot be transparent beyond Descemet's membrane because of the trabeculum. It will be seen from measurements that a trephine of 1.5 mm. or larger must go into clear cornea, that is, anterior to the end of Descemet's membrane, at least 0.5 to 0.75 mm. in order to avoid the ciliary body itself.

Ciliary processes should always be avoided if possible, but they are not detrimental unless they block the opening mechanically. It is not uncommon to find one or more processes in a well functioning trephine opening.

I do not believe that the practice of tilting the trephine to obtain a small hinge is very important. However, it is important to remember that the trephine blade may not be equally sharp around the whole circumference and that it is better to turn the trephine continuously in one direction than to rotate it back and forth. The continuous rotation insures a uniform cut.

Dr. Meek's suggestion of removing iris from the wound by suction is an interesting one. I have never tried it, but it sounds safer than fishing with forceps.

In the presence of definite uveitis, I should prefer to postpone a trephination until the eye became quiet. If the tension remained high during treatment of the uveitis, I should do repeated paracenteses.

Massage is very important. Since hearing Dr. Chandler's paper at a meeting at this Academy, I have followed his practice of applying continuous firm pressure, rather than alternate pushing with the fingers of the two hands. I believe that massage is contraindicated when there is no anterior chamber; the anterior chamber must be at least partially reformed before it is begun.

DR. RAYMOND E. MEEK: There is little on which I can take issue with Dr. Knighton. I think it is good practice to use retrobulbar injection and intravenous injections of dextrose, but I still feel that paracentesis helps in many cases of increased tension.

## Book Reviews

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**The Physiology of the Eye.** By Hugh Davson. Price, \$7.50. Pp. 451, with 301 illustrations. Philadelphia: The Blakiston Company, Division of Doubleday Company, Inc., 1949.

This concise, well written book is timely. There have been many new developments in the field of ocular physiology in recent years, and a survey of the field has been a difficult task, since this necessitated the reading of many scattered articles. This book presents an up-to-date, short, but in many places critical, summary of the biochemistry, physiology and optics of the eye. It is comprehensive and includes five sections: intraocular dynamics and the transparent tissues; the mechanism of vision; the muscular mechanisms; visual perception, and optics.

The author's style is lucid, somewhat discursive but yet compact. The exposition generally is simple and adequate. The book is intended primarily for students of ophthalmology and should be a distinct aid to the candidate qualifying for the examinations of the American Board of Ophthalmology. But it should be considered only as an introduction to the subject, and as a foundation for more thorough study of original articles. It should afford the practicing ophthalmologist a comprehensive review of the fundamentals of ocular physiology and refresh his memory on many aspects of basic physiologic optics that he may have forgotten.

The illustrations, most of which are diagrammatic, are simple and clear and serve their purpose well. The list of key references provided is a valuable representation of outstanding, pertinent original contributions. The alphabetical index is adequate.

HUGO L. BAIR.

**Current Therapy—1949.** Howard F. Conn, M.D., Editor. Price, \$10. Philadelphia: W. B. Saunders Company, 1949.

This book attempts to present the latest methods of treatment of a particular general medical condition as endorsed and currently used by competent medical authorities. It is not a review of the literature or an attempt to compile the numerous methods of treatment suggested for any one disease. Twelve consulting editors have selected a list of 200 leading American physicians who have contributed to the volume. It should prove a very useful book to the ophthalmologist who wishes to find out with the least expenditure of energy at least one method of treatment which is advocated by an expert in that particular field. The treatment of brucellosis, for example, is written by the chief editor. This article would be useful in the management of chronic cases of brucellosis with positive ocular involvement. The treatment of congenital syphilis is handled by 3 contributors, each one giving his individual method in conditions such as interstitial keratitis. It is a thoroughly practical book and is highly recommended for its concise and specific directions.

FRANCIS H. ADLER.

**Manual de oftalmología clínica y teorica.** By Prof. Manuel Marquez. Price, \$9.00. Pp. 272. México, D. F., Mexico: Cuadernos Oftalmologicos, 1949.

This is the first of four projected handbooks on clinical and theoretic ophthalmology, designed to cover all phases of the subject. This volume covers the essentials of general clinical ophthalmology, especially with reference to examination procedures and the correction of refractive errors. It is in a sense a condensed revision, with inclusion of the latest advances in the specialty of the author's previous work, now out of print, "Lectures on Clinical Ophthalmology." The forthcoming volumes will take up in greater detail many of the topics only briefly discussed here, as well as subjects of a more advanced character.

Chapter 1 opens with a brief history of ophthalmology, illustrated with photographs of the most eminent past masters of the specialty, and then goes on to a general consideration of the anatomy, embryology, physiology and pathology of the visual apparatus. This is presented in large, bold strokes, so to speak, and conveys in the short space of 22 pages a splendid over-all picture of the characteristics of the visual organ in health and in disease. Chapter 2 considers errors of refraction and accommodation. It covers the essentials of general optics as a preliminary to the study of the dioptric system of the eye; then follows a clear, succinct description of the various objective and subjective methods of measuring and correcting refractive and accommodative errors. This chapter is the longest one in the book and includes brief, pertinent references, for example, to corrected curve lenses, bifocal lenses, isekonic lenses and contact lenses. It touches also on muscular imbalances as they affect and are affected by refractive errors, the interplay of accommodation and convergence, the effect of some systemic diseases, such as diabetes, and of more localized diseases, such as glaucoma.

The remaining ten chapters cover the methods of general examination of the patient and specialized examination of the various parts, external and internal, including ophthalmoscopy, visual field tests, tonometry, slit lamp examination and fundus photography, with a description of the fundus camera of Dr. Rivas Cherif. This apparatus, hardly known in this country, takes excellent fundus pictures, as shown by several plates.

After an over-all study of general and special symptomatology, the author presents an excellent discussion of the general principles of treatment, local and systemic, by means of drugs, dietary regulation and physical agents, such as heat, electricity and diathermy. The application to the eye and to various structures affecting the eye, such as hypophysial tumors, of the radiations from the visible and the invisible portions of the spectrum is treated with some detail. A brief discussion of ophthalmic operations in general and the instruments necessary for such operations is included. The last chapter discusses the social and professional relation of the ophthalmologist to his patients, his colleagues, the pharmacist and the optician (optometrist). The author's expressed opinion is that refraction is part of a medical specialty and should be limited to the ophthalmologist.

The book is designed primarily for persons who have but little knowledge of ophthalmology, and it aims to give them a good over-all, working knowledge of the subject. It is definitely didactic: "Do this, and do it thus and so." In this way, it manages to include an excep-

tionally large amount of material in a scant 270 pages. The style is remarkably lucid, and the clarity of thought, simplicity and economy of expression are dominant characteristics. In examination procedures, as well as in methods of treatment and operation, the author's well known penchant for simplicity in everything, and for a minimum of instrumentation and intervention, is everywhere evident. The book is profusely illustrated with diagrams and photographs, both plain and colored.

Those having a reading knowledge of Spanish will derive profit and pleasure from a perusal of this work. Younger ophthalmologists especially will find the book of value, but seasoned practitioners will also find a number of topics treated in a new and stimulating manner.

JOSEPH I. PASCAL.

**The Practice of Refraction.** By Sir Stewart Duke-Elder. Fifth edition. Price not stated. Pp. 309, with 216 illustrations. 'St. Louis: C. V. Mosby Company, 1949.

This well known little book is now in its fifth edition. The fourth edition came out in 1943 and was reprinted three times, a fact which attests to its popularity. The character of the book has not been changed, but the material has been brought up to date. Recent views on the biologic determination of refractive errors has induced the author to regard the significance of myopia from a different point of view. The book covers all phases of refraction, from physiologic optics to the manufacture of glasses.

FRANCIS H. ADLER.

**Vision and the Eye.** By M. H. Pirenne. Price not stated. Pp. 182, with 9 illustrations and 4 plates. London: The Pilot Press, 1948.

This is an excellent introduction to the study of the physiology of vision. The author himself has made many valuable contributions to the physiology of the retina and has the ability to present the subject to the uninitiated so that it is understandable—a not too common quality among those who deal in pure science.

The first three chapters are largely anatomic and deal with the gross anatomy of the eye and the microscopic anatomy of the retina. The next two chapters describe some of the properties of the rods and cones and discuss spectral sensitivity curves. Chapters 5 to 8 deal with the nervous activity produced in the eye by the action of light and the minimum amount of light energy necessary for vision. It is shown that if one considers quantum fluctuations, the threshold corresponds very closely to the minimum amount of energy which can be presented to the eye, i. e., 1 or 2 quanta. Chapter 9 is an interesting and brief sketch of the eyes and vision of insects. Chapters 10 and 11 deal with the visual acuity of man and its variation with changes in light intensity. There are four chapters on color vision and its anomalies and a short chapter on binocular vision.

The book is well written and should be read by everyone interested in ophthalmology. With short, easily readable books like this, there can be no excuse for the persistence of total ignorance of the physiology of the retina which seems to be widespread, even in the best circles.

FRANCIS H. ADLER.

**Transactions of the American Ophthalmological Society.** Volume 46. Pp. 673. Philadelphia, American Ophthalmological Society, 1948.

This is probably the largest *Transactions* ever issued by the American Ophthalmological Society. A list of the papers presented follows:

Cataract and Tetany Produced by Parathyroid Deficiency During Pregnancy, Lactation and Menstruation, Dr. Donald J. Lyle  
Scleral Staphyloma and Retinal Detachment, Dr. Derrick Vail  
Herniation of the Anterior Hyaloid Membrane Following Uncomplicated Intracapsular Cataract Extraction, Dr. Algernon B. Reese

Effect of Dicumarol® on the Visual Fields in Glaucoma: A Preliminary Report, Dr. William P. McGuire

Keratoplasty for the Treatment of Keratoconus, Dr. Ramon Castroviejo

A Surgical Anatomy of the Superior Oblique Muscle, Dr. Walter H. Fink

A Simple Appositional Suture in Operations for Cataract, Dr. Charles A. Perera

Therapy of Ocular Inflammations Based on Immunologic Principles, Dr. F. Herbert Haessler and (by invitation) Dr. Herman A. Heise

Primary Malignant Melanoma of the Optic Disk: Report of a Case, Dr. Frederick C. Cordes and (by invitation) Dr. Michael J. Hogan

Dermoids and Epidermoids of the Orbit, Dr. Raymond L. Pfeiffer and (by invitation) Dr. Russell J. Nicholl

The Dupuy-Dutemps Dacryocystorhinostomy, Dr. Alton V. Hallum

Secondary Subjective Effects Produced by Prisms, Dr. Walter B. Lancaster

"Myopia Cures," Dr. S. Judd Beach

Mechanics of Intracapsular Cataract Extraction, Dr. David O. Harrington

Retinoblastoma in the Adult, Dr. Ralph O. Rychener

Familial Central and Peripapillary Choroidal Sclerosis Associated with Familial Pseudoxanthoma Elasticum, Dr. Banks Anderson

Surgical Procedures in Retinal Vascular Disease, Dr. Angus L. MacLean

Epidemiology of Epidemic Keratoconjunctivitis, Dr. Phillips Thygeson

Ocular Lymphomas, Dr. Parker Heath

Perineuritis Optica, Dr. Arthur J. Bedell

Aerobic Glycolysis of Corneal Tissue, Dr. P. J. Leinfelder

Study of the Effect of Retrobulbar Anesthesia on the Intraocular Tension and Vitreous Pressure, Dr. Harold Gifford Jr.

Choice of a Miotic Agent Following Retrobulbar Anesthesia, Dr. Harold G. Scheie and (by invitation) Dr. Gaylord Ojers

A New Instrument—The Harrington Tonometer, Dr. David O. Harrington

In addition to the papers presented, the following theses are contained in this issue of the *Transactions*:

Vascularization of the Cornea: Its Experimental Induction by Small Lesions and a New Theory of Its Pathogenesis, Dr. David G. Cogan

Enucleation and Allied Procedures: A Review, and Description of a New Operation, Dr. Jack S. Guyton

Amblyopia ex Anopsia: Observations on Retinal Inhibition, Scotoma, Projection, Light Difference Discrimination and Visual Acuity, Dr. S. Rodman Irvine

Evaluation of Night Vision, Dr. Phillip Robb McDonald

Surgical Treatment of Recurrent Pterygia, Dr. John S. McGavie

Direct Surgery of Underacting Oblique Muscles, Dr. John M. McLean

Ocular Effects of the Choline Esters, Dr. Kenneth C. Swan

The editor of the *Transactions*, Dr. Wilfred Fry, is to be congratulated on having produced a magnificent volume, which must represent an enormous amount of work.

FRANCIS H. ADLER.

**Medicine Throughout Antiquity.** By Benjamin Lee Gordon, M.D. Price, \$6. Pp. 818, with 157 illustrations. Philadelphia: F. A. Davis Company, 1949.

The author of this book is well known in ophthalmologic circles for his numerous articles on ophthalmologic history. This book endeavors to collect the methods by which medicine was practiced in antiquity. Part I, comprising 429 pages, deals with medicine before the era of the Greeks, and Part II, with Greek, Alexandrian and Roman medicine, together with a chapter on Talmudic medicine. It represents an enormous amount of work and, in addition to being interesting reading, should prove a valuable reference book.

FRANCES H. ADLER, M.D.

**Outwitting Your Years.** By Clarence William Lieb, M.D. Second printing. Price, \$2.75. Pp. 278; no illustrations. New York: Prentice-Hall, Inc., 1949.

This is a book for the lay public on how to grow old and like it. It is not a medical book on geriatrics and contains a short two pages on the ocular diseases of old age. The book is full of amusing anecdotes and will probably be useful to the patient who is resentful of the infirmities of old age.

FRANCIS H. ADLER, M.D.

## HEREDITARY MYOPIA

KARL C. WOLD, M.D.

ST. PAUL

THE THEORIES concerning the etiology of myopia are many and varied and have undergone a change as time has gone on. Von Graefe suggested that myopia was caused by subacute inflammation of the choroid and sclera. This theory has been disproved microscopically by the fact that the hyperemia, exudation and cicatrization found in myopia are only processes of repair which follow stretching and lacerations of ocular tunics. In 1610 Kepler stated the belief that the influence of near work, which requires accommodation and convergence, was an etiologic factor. Donders disproved this basic principle by showing that the highest grades of myopia may be found in illiterate persons and in people who never engage in close work. This theory was also disproved by Holm,<sup>1</sup> who made a thorough study of ocular refractive errors in the natives of Gaboon, French Equatorial Africa, one of the most ancient strains of the Negro race. These people showed tendencies in ocular refraction, from childhood to old age, more or less parallel with those found in the civilized world. The refractive variations were less conspicuous than among civilized communities, but this observation still bears out the theory that heredity plays the main role in myopia. Crisp concluded that three factors are concerned in the etiology of myopia, namely, (1) heredity, (2) nutrition and (3) the influence of study and close work, and that they may singly or jointly be responsible for the condition. This is a reasonable theory except that the second and third factors should be classified as contributory only.

Gates<sup>2</sup> gave the following source material on the etiology of myopia: Clarke (1925) suggested that myopia comes from stretching of fibroblasts in very early embryonic growth. He estimated that one child in a thousand is myopic by the sixth year but that at the age of 20 years 15 per cent are myopic. Parsons regarded congenital weakness of the sclera as hereditary and therefore a distinct factor in myopia.

Read at a meeting of the Minnesota Academy of Ophthalmology and Otolaryngology at St. Paul, Jan. 16, 1948.

1. Holm, S.: Heredity in Myopia, *Am. J. Ophth.* **21**:680, 1938.

2. Gates, R. R.: *Human Genetics*, New York, The Macmillan Company, 1946, vol. 1, p. 192; vol. 2, p. 934.



Watson (1934) found a pair of twins both of whom were myopic and in both of whom diabetes mellitus developed at 56 years of age. This finding is similar to a case in my experience (kindred 257), in which both mother and daughter had onset of diabetes and myopia at the age of 49.

Steiger's <sup>3</sup> article on the etiology of myopia is concerned with a controversy between H. Becker, of Munich, and himself (Zurich). At that time there were two prevalent theories about myopia: (1) the Lamarckistic, and (2) the Darwinistic. The Lamarckistic theory was based on the concept that myopia is simply an adaptation of the eye to present civilization. The Darwinistic theory assumed that the myopic eye is congenital and nothing can be done about it. Becker expressed the belief that myopia can be brought to a standstill by early correction, especially of the astigmatism, which is often only  $-0.25$  or  $-0.50$  D. Steiger adhered to the Darwinistic theory and stated the belief that correction of the refractive error, even in early childhood, will not prevent the progress of myopia.

Lindner <sup>4</sup> expressed the belief that myopia is not congenital but that the intensive use of the eyes, especially during the developmental years, has a great deal to do with its development. He stated the opinion that the rapid progress of myopia can be prevented by proper correction in early use. His theory of the causation of myopia is that there is a certain weakness of the sclera in the posterior segment of the eye near the papillary area. This weakness is caused by a change in the capillary blood vessels, due to constant edema in that region, which, in turn, is produced by a constant abuse of the visual organs in doing continuous close work.

Grunert <sup>5</sup> made the following observations on myopia: It is inherited as a normal variant in a biologic sense. It is a symptom of civilization, because in the domesticated being the extreme variants are not eliminated in the fight for survival but are preserved and propagated. He also claimed that there is a "physiologic inferiority" in the posterior portion of the eyeball in childhood. Grunert summarized his paper by saying that the hereditary tendency to *Dehnsucht* (stretching of the eyeball) in myopia consists mainly in the inheritance of an insufficient ciliary muscle and a particular weakness of the connective tissue of the sclera.

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3. Steiger, A.: Einige Bemerkungen zu Dr. Deckers Aufsatz: Klinische Beobachtungen über die Ursache der Kurzsichtigkeit, Berl. klin. Wchnschr. **56**: 419, 1919.

4. Lindner, K.: Neue Gedanken über die Entstehung der Kurzsichtigkeit, Klin. Monatsbl. f. Augenh. **103**:583, 1939.

5. van Grunert, Karl: Die Dehnsucht des Auges (Myopie) und ihre Behandlung, München, J. F. Lehmanns, 1934, pp. 8, 12, 16, 17 and 158.

The theory of compression of the globe by the extraocular muscles was advanced by von Arlt,<sup>6</sup> and later by Stilling.<sup>7</sup> It is possible that muscular contraction could injure an elongated globe but could not itself change the form of a normal globe with ordinary elasticity.

Hassner, and later Weiss,<sup>8</sup> decided that an optic nerve which is too short could pull on the back of the eye when the anterior part of the globe is turned in convergence. This traction would have the effect of producing a posterior staphyloma and consequent myopia. There has never been anatomic proof of this theory.

Stocker<sup>9</sup> stated that retinal changes, such as atrophy of the pigment epithelium, rods and cones and cystic degeneration, are determining factors in producing the stretching process, rather than changes in the choroid or the sclera. Heredity would still be the cause of myopia even though this theory were true.

All have seen cases in which myopia developed at 6, 10 to 12 or 18 to 20 years of age, roughly speaking, and have wanted to blame the influence of close work, greatly increased body growth or changes in calcium and thyroid metabolism. These cases reveal the hereditary pattern of myopia and show the influence of contributing factors only. The following conditions are the most probable contributing factors in the development of myopia: (a) Convergence. The action of the ciliary muscle in contraction pulls the choroid forward and breaks its insertions at the disk (as in myopic crescent). Binocular fixation necessitates rotation of the eyes inward, which is all the more pronounced as the point of fixation is nearer. The tighter this belt of internal and external rectus muscles becomes, the more elongation of the globe takes place, and the band might well interfere with the circulation in the vorticosae veins and thus cause congestion.

(b) Accommodation. The concomitant effect of accommodation, though not greatly exerted in a myopic person, may cause peripapillary alterations of the choroid, due to traction exerted on it by the longitudinal fibers of the ciliary muscle (tensor of the choroid), resulting in venous congestion of the uveal tract, a condition most favorable to permanent alteration of the deep membrane.

(c) Close work and reading. The bending of the head to such work, with the subject usually in a sitting position, and the corre-

6. von Arlt, C. F.: Ueber die Ursachen und die Entstehung der Kurzsichtigkeit, Vienna, Wilhelm Braunmüller, 1876.

7. Stilling, J.: Ueber das Wachsthum der Orbita und dessen Beziehungen zur Refraction, Arch. J. Augenh. 22:47-60, 1891.

8. Weiss, L.: Beiträge zur Entwicklung der Myopie, Arch. f. Ophth. 22 (pt. 3): 1-124, 1876.

9. Stocker, F. W.: Pathology and Anatomy of the Myopic Eye, with Regard to Newer Theories of Etiology and Pathogenesis of Myopia, Arch. Ophth. 30:476 (Oct.) 1943.

sponding sedentary state both contribute to congestion in the head, especially the eyes. This is especially true when the visual acuity is poor and an attempt is made to magnify objects by getting closer to them. Poor illumination also contributes to this factor.

(*d*) Abnormal function of calcium and thyroid metabolism. After considering all these opinions, theories and facts, one must conclude that myopia is caused by a congenital defect which exists in the resisting power of the sclera during the period the growth of the anteroposterior diameter of the eyeball. This defect is passed on through inheritance and is influenced by the aforementioned contributing factors.

#### TYPES OF MYOPIA

A. Anatomic Types: 1. Axial. Long eyeball with focus of parallel rays of light in front of retina.

2. Abnormal refraction. Excessive curvature of cornea or lens capsule.

B. Etiologic Types: 1. Acquired myopia. This type is found as a result of disease and trauma. Predisposing conditions are (*a*) changes in lens fibers associated with diabetes and intumescent cataract; (*b*) anterior staphyloma, caused by injury or disease of the cornea; (*c*) choroiditis and sequelae; (*d*) spasm of accommodation; (*e*) change in refractive index of the intraocular fluids, and (*f*) anterior displacement of the lens.

Weekers<sup>10</sup> reported the case of an 11 year old boy who was struck forcibly in the left eye. A  $-3.50$  D. sphere brought normal vision to this eye in twenty-four hours, and in one month a  $+1.00$  D. sphere was needed. The intraocular tension was very low as determined by palpation when the myopia developed. This transient myopia was attributed to relaxation of the zonule brought about by hyperemia and edema of the ciliary body, and the lowered tension, to absorption of the aqueous. Transient myopia also comes from chemical changes in the lens fibers, as after administration of the sulfonamide drugs and dinitrophenol. Acquired myopia constitutes less than 1 per cent of all types.

2. Inherited myopia. The genetic theory of myopic inheritance recognizes that each nucleus of the human ovum and sperm cell contains twenty-four paired chromosomes. The determining factors or genes are assumed to exist within the chromosomes like beads on a string. These genes go to make up the pattern of inheritance, which is classified as three types:

(*a*) A dominant character is one possessed by one of two parents of hybrids which appears in the hybrids to the apparent exclusion of the

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10. Weekers, R.: *Ann. d'ocul.* **178**:236, 1945.

antagonistic character. It is usually designated by a capital letter, such as B. A parent with a dominant factor will pass it on to 1 in 2 children, regardless of sex.

(b) A recessive character is one which is apparently not inherited by the hybrids, but is nevertheless latent and appears in their descendants, regardless of sex. For a child to have a recessive condition, each parent must contribute the same gene, which is designated by a small letter, such as *b*.

(c) A sex-linked recessive character is one which is carried from one sex through the second generation of the opposite sex to appear in the third generation of the original sex. This character is commoner in males than in females and is not passed on by affected males to their children, but their daughters transmit the character to half their sons. Myopia is one of the apparent thirty sex-linked traits in man.

TABLE 1.—*Incidence of Myopia in 231 Children Under 6 Years of Age*

Age Group	Myopia	Hyper- metropia	Normal
Premature.....	..	5	..
1½ hours to 7 days.....	2 (2.7%)	55	11
7 days to 1 year.....	1	9	8
1 to 2 years.....	1	12	..
2 to 3 years.....	1	20	1
3 to 4 years.....	4	21	1
4 to 5 years.....	3	33	1
5 to 6 years.....	3	35	4
Totals.....	15 (6.5%)	190	26

Stansbury <sup>11</sup> classified myopia into two groups: (1) primary myopia, which he termed a biologic variation, with clinical evidence that it is a healthy refractive state, and (2) secondary myopia, caused by disease of the eye in which a low grade chronic choroiditis is the primary cause.

#### INCIDENCE OF MYOPIA IN CHILDREN UNDER 6 YEARS OF AGE

According to Fuchs, about 5 per cent of infants are born myopic; 15 per cent are emmetropic, and the rest have a hypermetropia of 0.50 to 4.00 D.

Public health surveys in the United States and Great Britain have shown that the percentage of myopia increases from 1.1 per cent, at 2 years of age, to 10 per cent in Great Britain, but only to 7.8 per cent in the United States, by the twelfth year, the latter figure not including data on the newborn.

In a survey recently conducted by the Better Vision Institute, it was found that 7 per cent of all American children entering kinder-

11. Stansbury, F. C.: Pathogenesis of Myopia. *Arch. Ophth.* 39:273-299 (March) 1948.

garten are myopic, that 24 per cent are myopic on graduation from high school and that 31 per cent are myopic on graduation from college.

A personal review of all children seen during the last year who were under 6 years of age, including 73 newborn infants at the hospital nurseries, is presented in table 1. Each newborn baby was wrapped in a blanket and taken to a dark room. The nurse then held the lids open and the baby's eyes would almost immediately fix on the retinoscope light. Few of the pupils contracted even halfway, and the movement of the shadow was easily seen. Occasionally the pupils contracted moderately, but a satisfactory reflex was always obtained. The 5 pre-














	Normal, or nonmyopic, male
	Normal, or nonmyopic female
	Myopic female
	Myopic male
	Male - condition unknown
	Female - condition unknown
 	Ectopia lentis, male and female
	Twins
	Two marriages for one parent
  	Age, if significant, on first examination
2      12      3/12	

Chart 1.—Symbols used in charts 2 to 6.

mature babies, who were all hypermetropic, varied in gestation age from  $6\frac{1}{2}$  to 8 months. Two myopic infants were found among the 73 newborn infants, an incidence of 2.7 per cent. Fifteen of 231 children under the age of 6 years were myopic (6.5 per cent). Two sets of twins less than 7 days old were hypermetropic. One infant with myopia at birth had myopic parents, the father wearing a  $-0.75$  D. sphere and the mother wearing a  $-4.75$  D. sphere.

A careful study has been made of 258 kindred from my personal files in which at least two generations of proved myopia or of myopia in different and related families of the same generation were found. I have selected a few of the more interesting types, with explanatory notes for each kindred.

## REPORT ON THIRTEEN KINDRED

KINDRED 2 (chart 2*A*).—1. The trait showed sex-linked inheritance from the first to the third generation.

2. The pattern of dominance appeared for five generations in one branch.

3. In the fifth generation 1 male was myopic at birth.

4. In one branch of the third generation 10 nonmyopic members failed to alter the pattern of dominance in the fourth generation.

5. In the second generation 3 males died in young manhood of pulmonary tuberculosis, but none wore glasses.

KINDRED 35 (chart 2*B*).—This kindred presents a perfect example of sex-linked inheritance.

KINDRED 65 (chart 3*A*).—This pedigree is an unusual instance of sex-linked red-green color blindness with dominant myopia.

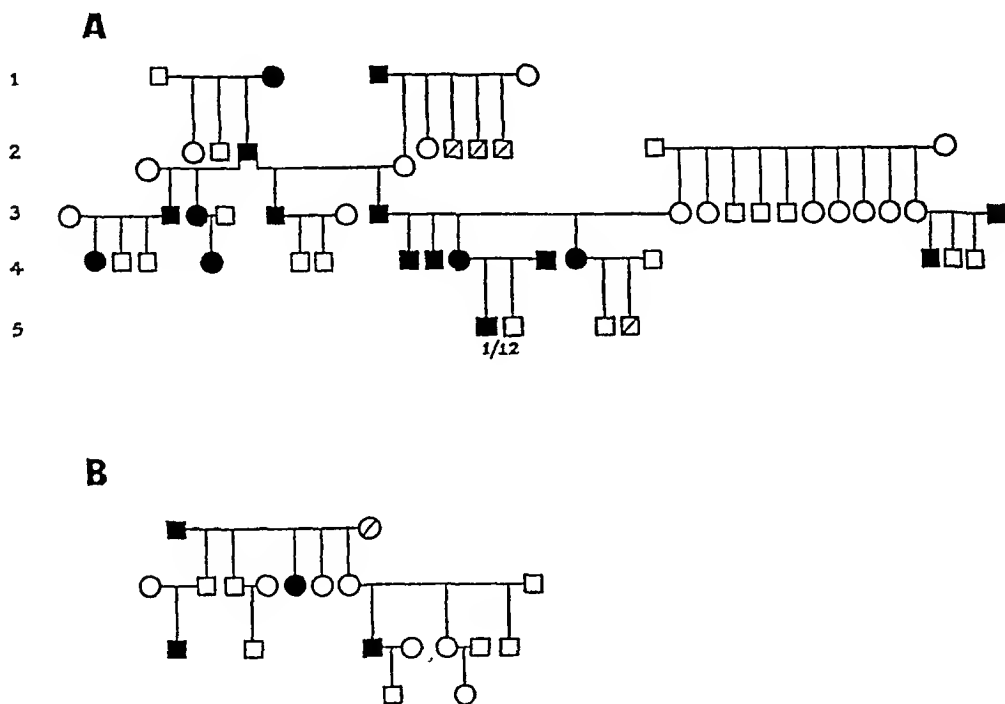


Chart 2.—*A*, kindred 2; *B*, kindred 35.

KINDRED 87 (chart 3*B*).—1. The unmarried twin has severe myopia; she wore glasses in the first grade and throughout school life sat in the front of the room. Her baby pictures show widely dilated pupils, and the general history indicates that she was myopic at birth.

2. The married twin has much less myopia but has carried the strain through to her son.

3. Although these twins are not identical, they have inherited myopia of different degrees.

KINDRED 122 (chart 3*C*).—This kindred illustrates three definite patterns of inheritance: (1) myopia transmitted as a dominant, in this kindred from the second to the third generation, and possibly to the fourth generation; (2) retinitis pigmentosa, inherited as a dominant in various stages; (3) color blindness, in 2 siblings, transmitted as a sex-linked character through the mother on the opposite side of the family.



KINDRED 136 (chart 4B).—1. Members of the family with ectopia lentis were myopic or nonmyopic, depending on whether they were looking through the lens or through the aphakic portion of the pupil.

2. This pattern shows true dominance for both myopia and ectopia lentis, with proved cases.

3. This kindred is a proved instance of inherited lenticular myopia, because the corrections for all myopic members were  $-7.00$  to  $-10.00$  D. sph. when they were looking through their lenses and from  $+8.0$  to  $+13.00$  D. sph. when they were looking through the aphakic portion of the pupil.

4. All myopic patients had either divergent strabismus or a high degree of exophoria.

The most interesting member in this family was T. C., in whom a transition from myopia to hypermetropia occurred. A brief of her case history follows.

Aug. 9, 1945: Refraction after mydriasis:

O.D.:  $-7.50$  sph.

O.S.:  $-4.50$  sph.  $\ominus -1.50$  cyl., axis 60

The patient was very comfortable until Feb. 1, 1947, when vision became blurred for both distance and close work.

July 15, 1947: Retinoscopic study with a mydriatic was done; the correction was as follows:

(a) Through lenses:

O.D.:  $-5.00$  sph.

O.S.:  $-7.00$  sph.  $\ominus -1.50$  cyl., axis 30

(b) Through aphakic portion:

O.D.:  $+10.00$  sph.  $\ominus +2.50$  cyl., axis 105

O.S.:  $+8.00$  sph.  $\ominus +2.00$  cyl., axis 75

On the same date a subjective test gave the following correction:

(a) Through lenses:

O.D.:  $-10.00$  sph.;  $\frac{9}{100}$

O.S.:  $-7.00$  sph.;  $\frac{9}{30}$

(b) Through aphakic portion of lenses:

O.D.:  $+13.00$  sph.;  $\frac{9}{15} +2$

O.S.:  $+13.50$  sph.;  $\frac{9}{15} +2$

July 16, 1947: Because plus lenses gave better vision, the following correction was prescribed:

O.D.:  $+12.50$  sph.;  $\frac{9}{15} +2$

O.S.:  $+13.50$  sph.;  $\frac{9}{12} +2$

The patient looked through the center of these lenses, while with the old minus lenses she was forced to turn the head to one side and look through the margin of the crystalline lenses in order to get clearer vision.

Aug. 20, 1947: Lenses prescribed in July caused occasional nausea and discomfort; so with the opening of school the following prescription was given:

O.D.:  $+12.50$  sph.; with  $+2.50$  sph. added

O.S.:  $+13.50$  sph.

Oct. 10, 1947: The patient had been assigned to a sight-saving class but preferred regular class and was completely comfortable with bifocal lenses.



KINDRED 163 (chart 5 *A*).—1. A myopic female was married twice, each time to a nonmyopic male.

2. Dominance is more prominent on one side of the family because of recessive genes in the male on that side.

KINDRED 174 (chart 5 *B*).—1. Myopia is recessive except for the last family in the second and third generations.

2. Despite myopia in the female of the first generation, all evidence on the unknown first generation side points to the recessive inheritance.

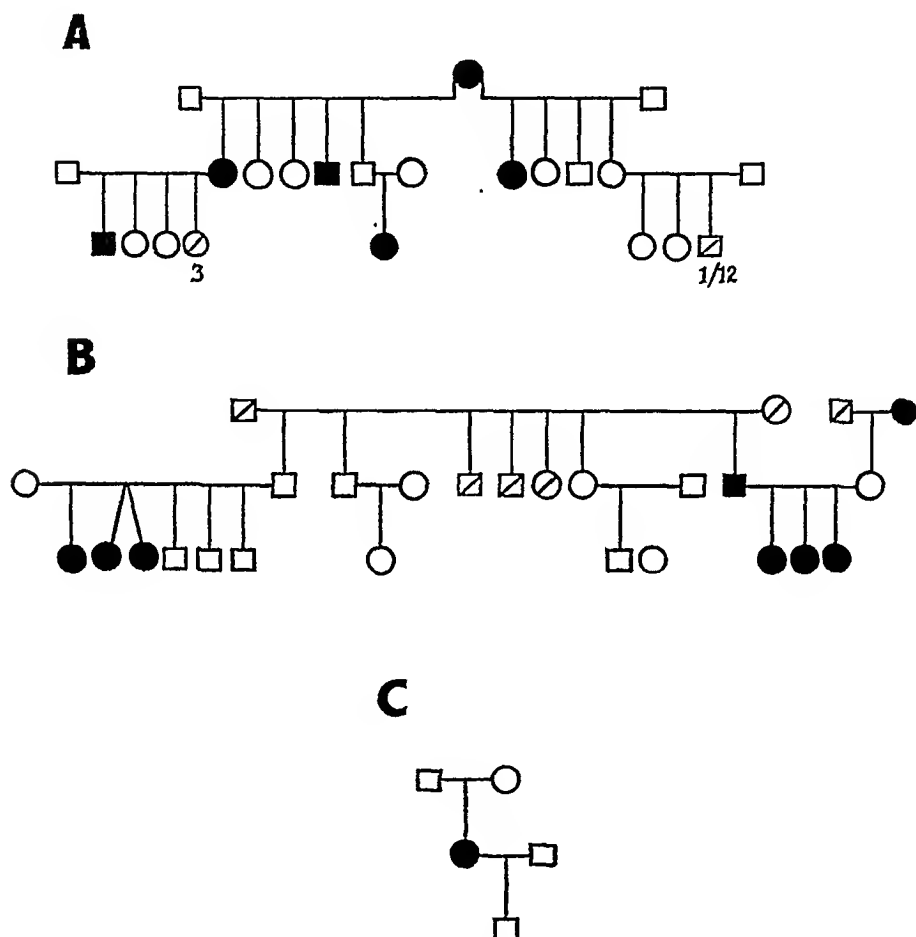


Chart 5.—*A*, kindred 163; *B*, kindred 174; *C*, kindred 256.

3. Identical twins in the third generation have myopia, although in one twin it is moderate and in the other severe.

4. The myopic sister of twins had scarlet fever at the age of 7; is subnormal mentally and had a glandular disturbance, the significance of which is doubtful.

KINDRED 256 (chart 5 *C*).—1. There was no history of myopia in the family.

2. In January 1940 the affected member was given a correction of +5.00 sph. for each eye, with +1.00 sph. added.

3. For eight months in 1940 he had recurrent herpetic ulcers of the left cornea and was hospitalized three times.

4. November 1947: The following correction was given:

O.D.: +5.00 sph., with +1.75 sph. for reading

O.S.: -1.75 sph.

5. This patient has a typical case of acquired myopia from corneal disease, a not infrequent occurrence.

KINDRED 253 (chart 6 *A*).—1. The unknowns in the first generation undoubtedly produced a dominant strain, extending to the fourth, and possibly to the fifth generation.

2. When a female in the third generation married a male with decidedly no tendency to myopia, 2 of 4 offspring were still myopic.

3. In the fourth generation the myopic female to the right has inherited the trait as a recessive, through the mother, whose antecedents were unknown.

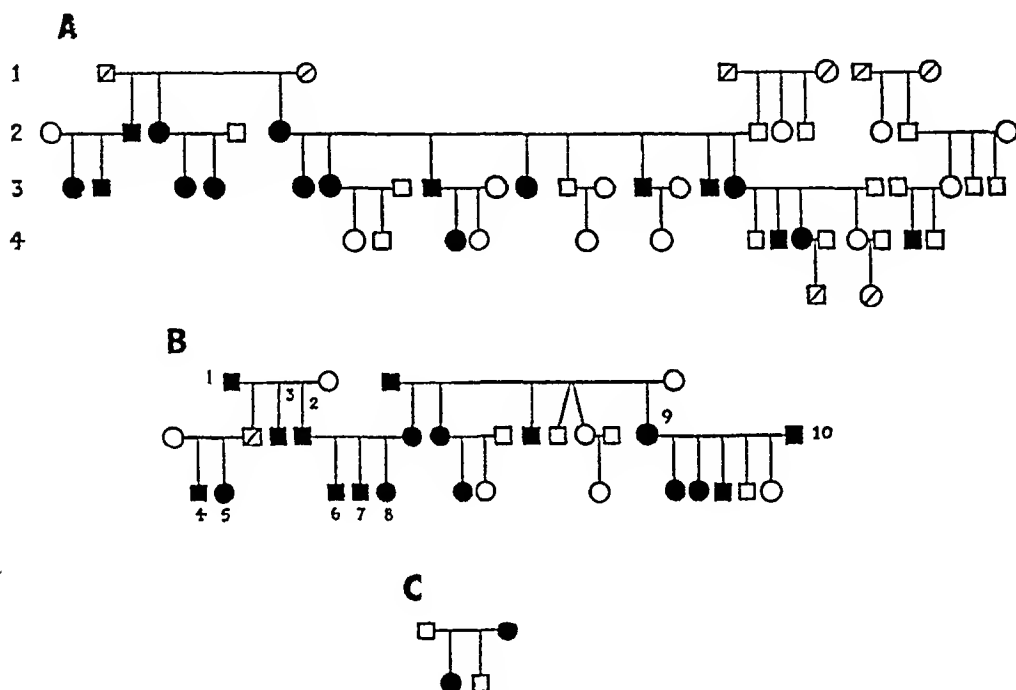


Chart 6.—*A*, kindred 253; *B*, kindred 255; *C*, kindred 257.

KINDRED 255 (chart 6 *B*).—1. Severe myopia was found in 1, a man who also had incipient cataract in each eye before death.

2, who was a minister, had mild myopia of less than 1 D.

3 the monocular diplopia, due to changes in the lens, and the myopia showed the same incidence as in his father.

4. Correction of -5.00 sph. was given for each eye. Myopia developed early in this boy (4). Correction for the sister (5) was -6.00 sph. for each eye. This girl's myopia was similar to her brother's.

5. These three siblings (6, 7 and 8) show how the inheritance of myopia varies in the same family. (6) Correction was 12.00 sph. for the right eye and -13.00 sph. for the left eye. (7) Correction was -5.50 sph. for each eye. 8 had mild myopia.

6. Correction was -8.00 sph. for the right eye and -9.00 sph. for the left eye.

7. Moderate myopia in 10 and rather severe myopia in his wife resulted in myopia in 3 of his 5 children.

8. Two affected males in the first generation produced the dominant pattern through three generations.

9. Only the twins in the second generation show the recessive trait, with the condition of one unknown.

10. Dominance is definitely shown in the union of two main families.

KINDRED 257 (chart 6 C).—Mrs. M., aged 49, shows an interesting hereditary history of myopia. Her vision became blurred three years ago and had been much worse during the last year. At the age of 25, she wore a correction of  $-0.62$  sph.

TABLE 2.—*Comparative Data in Incidence of Myopia in Children of Myopic and Nonmyopic Parents*

A. Neither parent myopic		}	Purely recessive
Males			
65 myopic.....	230 myopic		
201 nonmyopic.....	415 nonmyopic		
Females			
165 myopic.....	35% myopic		
214 nonmyopic.....			
B. One parent myopic		}	Dominant
Males			
124 myopic.....			
180 nonmyopic.....			
Females			
185 myopic.....			
139 nonmyopic.....			
C. Both parents myopic		}	309 myopic 319 nonmyopic 49% myopic
Males			
11 myopic.....			
3 nonmyopic.....			
Females			
9 myopic.....			
4 nonmyopic.....			

for each eye but had not worn these glasses for the last two or three years. At the age of 49, twenty-five years later, she was given the following correction:

O.D.:  $-3.00$  sph.  $\ominus -1.50$  cyl., axis 90

O.S.:  $-4.00$  sph.  $\ominus -1.00$  D. cyl., axis 90

In addition to the myopia, examination revealed diabetes, which was well controlled by insulin, and radial opacities in each lens.

The patient's mother had gone through the same sequence at the same ages, and she eventually had had both cataracts extracted.

This case presents an exception to disease as the cause of acquired myopia in that there was a definite pattern of inheritance of both myopia and diabetes.

For comparative study a tabulation was made of children who had nonmyopic parents but who were included in the kindred with myopia (table 2). Similarly, those with myopia in one or both parents were studied and classified.

# TREATMENT OF MYOPIA

A careful and thorough refraction, with consideration given to accommodative power, muscle balance, age and occupation, is the best treatment for hereditary myopia. Proper light, position of the head in relation to reading material, outdoor recreation, well balanced diet and choice of occupation are important factors. All treatment such as stimulation of the ciliary muscle, administration of calcium for the sclera and thyroid for correction of low metabolic rate and medication for choroiditis cannot alter the hereditary pattern and is therefore futile.

Treatment for acquired myopia includes use of ordinary or contact lenses, cataract extraction, penicillin therapy, local treatment of the eyes and insulin, as indicated. Even in cases of hereditary excessive curvature of the cornea, contact lenses will reduce the amount of myopia and often eliminate astigmatism.

## SUMMARY AND CONCLUSIONS

There are two types of myopia: (1) hereditary, which may be dominant, recessive or sex linked, and (2) acquired, due to disease or trauma.

Dominant myopia is the most prevalent type, followed closely in frequency by the recessive type, the sex-linked recessive form being the least common (table 2).

Myopia was found in 2.7 per cent of newborn infants under 7 days of age and in 6.5 per cent of all children up to 6 years of age.

In a survey of 257 kindred with myopia, the following data were obtained:

1. With neither parent myopic, 230 of 645 children, or 35 per cent. were myopic. In these children the myopia was purely recessive.
2. With one or both parents myopic, 309 of 628 children, or 49 per cent. were myopic. In these children the trait was dominant.

## OCULAR ALLERGY

Allergic Phenomena Affecting the Eye and Its Adnexa

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SAN ANTONIO, TEXAS

THE OPHTHALMOLOGIC aspects of allergy have occupied a prominent place in the development of knowledge of the subject from the beginning. A number of widely different ocular disorders, both external and internal, are of allergic origin. Dermatitis of the eyelids and conjunctival edema, vernal conjunctivitis, conjunctival folliculosis, subconjunctival hemorrhage, retinal hemorrhage and optic neuritis may be mentioned as ophthalmic conditions that are often due to allergy. Substances to which a person is specifically sensitized, such as plants and their pollens, cosmetics, nail polish, soaps, shampoos, drugs, hair dyes and emanations from fur, feathers and animals, are a few of the great variety of agents which may produce contact dermatitis. Lacquers, paints, paint solvents, refrigerants and other volatile substances used in industry are also frequent offenders. Aside from the local reaction which such agents may provoke, they may, by oft repeated inhalation, give rise to a variety of internal disorders, such as optic neuritis, ocular palsies and paralyzes due to lesions produced in the central nervous system. The effects of the reaction-producing substances, or allergins, vary with the individual patient, some persons being more easily affected by them than others. The sulfonamide drugs, as well as penicillin, introduced into the conjunctival cul-de-sac produce reactions in a high percentage of patients, the incidence of such reactions being so great that some ophthalmologists have discontinued their local use in the eye altogether.

Reactions may occur in the eyelids or conjunctiva as an associated manifestation of allergic rhinitis, or hay fever; the red, engorged conjunctiva and swollen eyelids being a familiar part of the nasal syndrome. Protein substances and toxins generated in the growth of bacteria and pathogenic molds or their spores are generally accepted as being capable of producing allergic reactions in the skin of the eyelids or in the conjunctiva. Sometimes the reaction produced in the eyes from contact with commonplace substances may be so great as to

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constitute a serious economic handicap. I have personally observed 3 persons in the bakery business who were so intensely sensitive to wheat products (flour) that their continuance in this occupation was impractical, because of the persistent reactions in their eyes. Instances of severe local reactions from atropine and homatropine have come under the observation of almost every ophthalmologist. When such reactions occur, they usually come on within a few minutes after the introduction of the drug into the eye, the reaction being so severe in some instances the eyes may be closed by swelling within a few minutes. Vesiculation in the skin of the eyelids tends to occur when the reaction is slow in developing, this being most likely to occur if repeated consecutive applications of the offending drug are persisted in, and if its use is long continued a chronic eczematoid state may be produced in which there is marked serous exudation. In postoperative care of cataract patients, in which atropine is commonly employed, the appearance of irritation and persistent swelling of the eyelids as a prominent feature should suggest sensitization to atropine. Persistent, unexplained conjunctival irritation may be due to sensitization to some particular drug used daily in or about the eyes. Physostigmine and pilocarpine drops, commonly employed in the treatment of glaucoma, often produce vascular reactions in the eye, especially after use for several weeks. This type of reaction is considered by most authorities as a toxic, rather than an allergic, reaction. Almost without exception, patients with glaucoma reach a point where physostigmine produces local irritation in the eye and must be discontinued. Pilocarpine produces a similar reaction, but when the patient acquires sensitivity to one of these drugs a change from one to the other may be made without perpetuating the irritation. Therefore, the simultaneous use of these drugs as eye drops, which is sometimes advised, is open to a degree of objection. Carbachol, a new drug used in the treatment of glaucoma, may be a valuable substitute in cases in which both physostigmine and pilocarpine have induced local reactions, but carbachol, like physostigmine and pilocarpine, may produce local reactions in the eye. A change in the  $p_H$  of the tears is apparently associated with the production of such reactions. The higher the  $p_H$  the more likely is the reaction to develop. This has been taken advantage of from the practical standpoint by using citric acid in the form of eye drops or ointment in conjunction with the miotics to lower the  $p_H$  (raise the hydrogen ion concentration) of the fluids in the conjunctival cul-de-sac. There may also be a direct effect of the acid on the conjunctiva, as the reaction level of this tissue appears to be raised by such additions. It may be that other hydroxy acids are equally efficacious in this respect, but my clinical experience has been limited to only one, citric acid. I have had no experience with

the new antihistaminic substances, either prophylactically or therapeutically, in such reactions.

Eosinophilia in the conjunctival secretions does not occur in physostigmine or pilocarpine conjunctivitis but does occur in atropine and homatropine conjunctivitis, a point of difference the significance of which has been somewhat controversial. The opinion has been expressed in some quarters that, while atropine may produce an allergic reaction in the eyes, as evidenced by the occurrence of eosinophils, the absence of these cells in pilocarpine and physostigmine conjunctivitis would indicate that the reaction produced by the latter drugs is toxic rather than allergic. Preservatives used in commercial eye lotions have occasionally been observed as the cause of persistent ocular irritation, which disappears when the wash is discontinued. Chlorobutanol heads the list of offenders in my experience. Aqueous acriflavine solution, which is one of the most efficient and least irritating antiseptics for local use in the eye, occasionally produces a vascular reaction, with associated papillary swelling and the picture of an allergic reaction. One of the newer drugs which has found great favor as a conjunctival antiseptic is sodium sulfacetimide, which may, like other drugs, produce a local reaction in the eye. Many drugs have no adverse effect in the beginning but produce reactions after a time, as a cumulative effect or as a result of a change in the reactive capacity of the patient's tissues, in which they become less tolerant to the drug. This, in turn, is apparently influenced by the  $p_H$  of the tears.

Edema of the eyelids and urticarial lesions about the eyes may occur as an acute allergic phenomenon due to the ingestion of a food or drug to which the patient is specifically hypersensitive. Optic neuritis and retinal hemorrhages have been attributed to allergic reactions by Hansel<sup>1</sup> and Wittich<sup>2</sup> and are regarded as counterparts of urticarial lesions elsewhere on the body.

Stings from a variety of insects, such as mosquitoes and bees, are also productive of acute edematous lesions of the eyelids, owing in part to the chemical which they inject and also, at least in sensitized persons, to protein bodies contained in the poison. There are instances on record in which constitutional reaction associated with such stings have been fatal, probably as a result of allergic shock.

Acute or chronic vascular engorgement of the conjunctival vessels may be the result of exposure to an unsuspected atopic reagin and may be the cause of long-standing conjunctival hyperemia, or red eyes.

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1. Hansel, F. K.: *Allergy of the Nose and Paranasal Sinuses*, St. Louis, C. V. Mosby Company, 1936.

2. Wittich, J. W.: *Journal-Lancet* 65:249. 1945.

The precise disease picture produced in allergic reactions in the eye depends largely on which ocular tissue is acting as the shock organ:

Physical allergy is that form of allergic reaction produced in susceptible persons by exposure to heat, light, cold or trauma. Pure physical allergy is considered rare but as an exaggerating factor added to other allergic reactions is often of importance. The release of histamine-like substances in the skin is considered the most probable mechanism involved in the production of physical allergy. In the Southwest it is not uncommon to encounter patients with chronic conjunctival irritation which is apparently due solely to the effect of heat and bright sunlight. My personal belief is that this type of physical allergy is a prominent factor in pterygium, though almost certainly other, equally important, factors, such as a shift in the hydrogen ion concentration of the tears to the alkaline side, which operate in the production of this condition. Recurrence of pterygiums following adequate surgical removal is not infrequent in the Southwest, most probably because no environmental change is made in the physical surroundings after the growths are removed. A continuance of the underlying factors originally producing the hyperplastic change in the conjunctiva will explain the recurrence of pterygiums in most persons. The use of lenses which afford a degree of protection from infra-red rays, as well as from the ultraviolet and visible light, will afford a degree of protection against these physical factors and are to be considered as part of the postoperative care of patients with pterygium, even though no refractive error is present. A persistent highly alkaline reaction of the tears no doubt favors the return of pterygiums. The use of a mild acid type of eye lotion will, in my opinion, act as a deterrent or an inhibitor to the return of these growths. The objection to aqueous lotions is that their effect is fleeting, lasting on an average less than two minutes. Ointments of citric acid in aquaphor® (an oxycholesterol-petrolatum ointment base) mixed with petrolatum are more lasting, and on the whole more advisable, but from the patient's standpoint, less so because of the greasiness and blurred vision associated with their use.

"Spring catarrh," or vernal conjunctivitis, frequently encountered in children, is usually, if not always, associated with persistent exposure to atopens. It is characterized by chronic irritation with catarrhal discharge and follicular hypertrophy. The severity of the reaction in the eyes is governed by the degree of susceptibility in the patient, the quantity or dose of the atopen, the persistence of contact with it and its degree of solubility in the tears, the last factor, in turn, being influenced by the degree of alkalinity of the tears. It will be recalled that the Calmette reaction for tuberculosis, or the so-called ophthalmic



reaction, was one of the early reactions to tuberculin elicited in persons sensitized to tuberculin (tuberculoxin), that test being performed by dropping a tuberculin solution into the eye. A more or less violent vascular response, produced in the eye of the sensitized person, constituted a positive diagnostic reaction. The test was a crude one, and not without danger to the eye. Fortunately, this test is no longer used on the human subject, as far safer and more exact diagnostic procedures have supplanted it.

In follicular or in vernal conjunctivitis, the discharge from the eye is heavy with eosinophils, a fact of importance in differential diagnosis of follicular conjunctivitis and other conditions likely to be confused with it, such as trachoma. In general, it may be said that the eosinophil is the key cell in the cytologic diagnosis of allergy of the eye, as it is in allergic rhinitis—just as edema may be said to be the characteristic lesion of allergy. Trained observers will not be satisfied with the occurrence of a few pink-stained leukocytes in the smear; to be diagnostic, the cells must contain visible eosinophilic granules.

Herbert<sup>3</sup> in 1903 noted the importance of the eosinophil in the diagnosis of vernal conjunctivitis but did not associate the finding with atropism or allergy. This came later. Basophilic leukocytes were also noted as being increased in allergic conjunctivitis and vernal catarrh by Thygeson,<sup>4</sup> who observed that they sometimes outnumbered eosinophils in the latter condition. He further stated that the presence of basophils in large numbers appeared to have as definite a diagnostic significance as that of eosinophils. Fragmentation of eosinophils and basophils is frequent in the discharge of allergic conjunctivitis; therefore, free eosinophilic or basophilic granules are often seen in the secretions. The intact cells are not always easily demonstrated, but persistence will almost always be rewarded with success. The cells in question are more easily demonstrated in conjunctival curettings or scraping than in the free secretions. Curettage is accomplished by anesthetizing the lids by instillation of one of the usual anesthetics and using a Myerhofer curet to obtain the surface cells. Excessive curettage is neither necessary nor advisable. The material for examination is spread on an ordinary glass slide and fixed by drying in the air. Polychrome stains, such as the Wright or the Giemsa stain, are commonly employed in staining such preparations. My colleagues and I have preferred to make a percentage count of the leukocytes when possible, as it gives an excellent check on the clinical course of an

3. Herbert, H.: *Brit. M. J.* 2:735, 1903; 2:1232, 1907.

4. Thygeson, P.: *Cytology of Conjunctival Exudates*, The Association for Research in Ophthalmology, 15th Annual Report, pp. 7, 1946.

allergic reaction and is a good index of the efficiency of any particular type of therapy. This is easily accomplished by inserting a cardboard diaphragm in the microscope eyepiece, in which a 0.5 cm. or, if preferred, a 1 cm. square window has been cut. Such percentage counts are made in nasal as well as in ophthalmic smears; 50 to 100 cells are counted if they are present in sufficient number, fragmented cells being disregarded. Often, the percentage in ophthalmic smears must be computed on a total count of as few as 25 cells. A decrease in percentage of eosinophils usually means clinical improvement.

"Generally speaking, polymorphonuclear neutrophils are characteristic of bacterial infections, mononuclear cells of virus infections, eosinophiles and basophiles of allergy." <sup>5</sup>

Phlyctenular conjunctivitis and keratoconjunctivitis are at present regarded by most authorities as an allergic response to bacterial protein from a focus of infection, such as might occur about the teeth or in the tonsils or the nasal accessory sinuses. Such attacks not infrequently follow acute infections of the upper respiratory tract, such as an ordinary cold or influenza, the theory being that the eye has previously been rendered hypersensitive to the bacterial toxin or virus in such infections and a second exposure to a toxin from the same or a closely related strain of bacteria produces the local explosion in the eye. No eosinophils occur in the conjunctival secretions in this disease. Bacterial toxins or proteins apparently do not have the property of calling forth an eosinophilic response in tissues sensitized to them. I have recently observed a severe bilateral phlyctenular keratoconjunctivitis in a 16 year old girl in which the corneal infiltrate predominated; this condition resisted all measures, including tonsillectomy, but responded promptly to hyposensitization with house dust and ragweed pollen.

A clear concept of what is meant by the Arthus and Shwartzman phenomena is essential to a proper understanding of what takes place in certain allergic reactions. Briefly stated, they may be defined as reactions occurring in a previously sensitized structure after the second administration or absorption of the original type of antigen which produced the initial sensitization. When a bacterial antigen acts as the sensitizing agent, the antigen producing the second reaction may come from either an identical or a closely related strain of bacteria.<sup>5</sup>

According to Carleton,<sup>6</sup> up to 1943, there were reported 46 cases of lenticular cataract occurring in persons with chronic neurodermatitis in which the relation was explainable on an allergic basis. The change in the lens usually comes in the fourth decade of life.

5. Gill, E. K.: *Texas State J. Med.* 43:330-334 (Sept.) 1947.

6. Carleton, A.: *Brit. J. Dermat.* 55:83, 1943.

Tuberculosis, so far as the ocular response is concerned, may be considered a disease in the allergic category. The nucleoprotein or tuberculin elaborated in the growth of the tubercle bacillus may act as a foreign protein to sensitize the eye, and later, with continued absorption, it acts as a secondary allergin to produce any one of a variety of inflammatory lesions in the eye. Eosinophilia is not produced in the secretions of the eye by the lesions of ocular tuberculosis. In tissue sections a lymphocytic response and giant cells are seen, but in the secretions of the tuberculous eye there is no diagnostic cytologic picture. The fact that the organism is sensitized to tuberculoprotein or to tubercle bacillus toxin can be demonstrated by any one of several well known tests—the patch test, the scarification test or the intradermal injection of some form of tuberculin. The most frequently used tuberculins are old tuberculin and the purified protein derivative of tuberculin. Extremely minute quantities of tuberculoprotein will precipitate reactions, local, general and focal, in sensitized persons. Great caution must be exercised in their use, as the employment of too large doses in the injection test may lead to severe and disastrous focal reactions in an eye which is sensitized to this substance. The tuberculin used in testing, regardless of its type, must be enormously diluted, for once it is introduced into the body it cannot be withdrawn nor can its effect be mitigated. No one should use tuberculin as a diagnostic agent unless thoroughly familiar with its potential dangers. The patch test is easily applied, more easily controlled and far safer in all respects, and is considered best for the occasional investigator, though it is perhaps a little less desirable from the diagnostic standpoint than the injection test, as it lacks the quantitative features of the latter.

In syphilis the reactions induced in the eye, such as iritis, iridocyclitis and keratitis, are considered allergic manifestations, due to the infected person's becoming sensitized to his own strain of syphilitic toxin or antibodies—certainly to some protein-like substance elaborated in the course of the disease. The mechanism of production is similar to that of tuberculous lesions of the eye.

Elschnig,<sup>7</sup> and later Wood,<sup>8</sup> developed the theory that sympathetic ophthalmia was an allergic manifestation due to disintegration of uveal pigment and its absorption, with resultant autosensitization. Further absorption of uveal pigment precipitates a secondary reaction wherever the particular type of pigment (melanin) occurs. A sterile or allergic

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7. Elschnig, A.: *Arch. f. Ophth.* **75**:459, 473, 1910; *ibid.* **76**:509-546, 1910; *ibid.* **78**:549-583, 1911.

8. Wood, A. C.; *Arch. Ophth.* **45**:557-563, 1916; *ibid.* **47**:161, 1918; *ibid.* **46**:503-517, 1917; *Immune Reactions Following Injuries to Uveal Tract*, J. A. M. A. **77**:1317-1322 (Oct. 22) 1921.

reaction is produced in the uveal pigment layer of the opposing, or sympathizing, eye by this mechanism. Other observers supported the view of Elschnig and Wood and Knapp.<sup>9</sup> To any one who has seriously investigated the relation of uveal pigment to sympathetic ophthalmia the relationship is quite evident, and so striking that the logical conclusion seems to be that, while sympathetic uveitis may not be entirely an allergic disease, there is an allergic phase in which a definite sensitization to uveal pigment exists. This may be further substantiated by a complement fixation test of the patient's blood, in which uveal pigment is used as the antigen. This test does not lend itself to routine clinical use because of its complex nature, but it is interesting from the investigative standpoint. Local hypersensitiveness to injected uveal pigment and clinical response to pigment used therapeutically are additional substantiating evidence to support the belief that there is an allergic phase of this disease. Hypersensitiveness to uveal pigment is preceded by a phase in which bacterial toxins pave the way and prepare the eye for sensitization by producing foci of inflammation in the choroid. Such foci arise as a result of the eye's having become previously sensitized by bacteria or toxins from the same or a closely related strain of organisms elaborating the original sensitizing allergin or toxin. The reaction which accompanies such pathologic changes in the choroid of the exciting eye is sufficient to cause disintegration and solution of a certain amount of uveal pigment, which is absorbed and sensitizes the eyes—both of them—to uveal pigment. Subsequent absorption of pigment, even remote, precipitates a secondary reaction of an allergic nature, which is designated as sympathetic ophthalmia. The reaction in the first, or exciting, eye is more correctly designated sympathogenic ophthalmia or uveitis. In eyes enucleated prior to the actual development of sympathetic ophthalmia, characteristic microscopic changes exist, consisting of foci of lymphocytic infiltration with associated giant cell formation. Eosinophils have been found in the choroid in practically all my sections of eyes removed as the exciting eye in cases of sympathetic ophthalmia, but not in sufficient number to be unequivocally diagnostic of allergy.

Further substantiating evidence of the specificity of uveal pigment in sympathetic ophthalmia is obtained by histologic examination of the point of injection in the cutaneous test, with the demonstration of phagocytosis of pigment particles in the excised area of injection after a two week interval has elapsed, as noted by Friedenwald,<sup>10</sup> and,

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9. Wood, A. C., and Knapp, A.: *Arch. Ophth.* **51**:560-565, 1922; *Bull. Johns Hopkins Hosp.* **33**:419-425, 1922. Knapp, A.: *Tr. Am. Ophth. Soc.* **22**: 256-268, 1924.

10. Friedenwald, J. S.: *Am. J. Ophth.* **17**:1008, 1934.

further, by study of the opsonic index with pigment, as recommended by Henton.<sup>11</sup>

In the type of uveitis of a nonsympathetic nature due to focal infection, we have concluded from our investigation with uveal pigment, both diagnostic and therapeutic, that in most cases this type of uveitis has essentially the same immunologic background as has sympathetic ophthalmia.<sup>12</sup>

The question arises as to why one person will respond with an allergic reaction of the eye from any cause and another, with apparently the same clinical background, will fail to exhibit such reaction. This is a question which must be answered largely speculatively, but certain factors are apparently of some importance in formulating an answer.

Heredity plays an important part in certain allergic disease of the eye. Follicular conjunctivitis is one of these. It is not at all uncommon to encounter several children in the same family who are suffering from conjunctival folliculosis, in the same or in varying degrees. Not infrequently one of the parents will give a history of similar trouble in childhood. It is easy in such instances to make the mistake of considering such ocular lesions as trachomatous and assuming that the children are all infected with the trachoma virus. Hay fever, or allergic rhinitis, is a frequent accompaniment of follicular conjunctivitis, revealing the patient's general allergic tendency. The spontaneous disappearance of conjunctival folliculosis at puberty is strongly suggestive of an influence of the sex glands, which take on certain changes at that period.

Alkalization of patients with certain allergic manifestations, such as hay fever, accentuates the symptoms; and it has been observed clinically that when a patient is hovering on the verge of an allergic explosion, such as allergic rhinitis, the reaction can usually be precipitated by the internal administration of alkalis. I have cause to believe that in such patients the body chemistry is too far on the basic, or alkaline, side, even though this shift may be very slight and represented by only a minute variation in the hydrogen ion concentration ( $p_H$ ) of the tissues. It is further believed that the difference in the  $p_H$  (acid-base balance) inherent in different persons may explain why in one person a certain disease, such as conjunctival folliculosis or even sympathetic ophthalmia, will develop and in another it will not, even though all other factors are apparently operating equally. The use of an acid ash diet or the ingestion of diacid salts and even mineral

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11. Henton, H. C., Opsonic Index for Uveal Pigment in Treated Patients, *Arch. Ophth.* **17**:113-116 (Jan.) 1937.

12. Gill, William D.: *South M. J.* **23**:885-894, 1930; *ibid.* **34**:959-968 (Sept.) 1941; *Ann. Otol., Rhin. & Laryng.* **44**:486-492 (June) 1935.

acids, such as hydrochloric acid, has a salutary influence on the course of most allergic states, while the employment of alkalis and alkaline ash foods has the opposite effect, an observation which may be advanced as further support of this belief.

Verhoeff and Lemoine<sup>13</sup> described a type of allergic reaction in the eye which they termed phacoanaphylactic endophthalmitis, in which the patient is sensitive to lens protein. The hypersensitiveness to lens protein is said to be present in 8 to 10 per cent of all persons. The reaction occurs when lens protein is allowed to remain in the eye after the lens capsule is broken, as would occur in a combined linear cataract extraction, in needling operations to produce absorption of juvenile cataract or in certain types of accidental trauma to the eye. The reaction varies in degree, being slight in some instances and intense in others; often it is sufficiently severe to cause loss of the eye. Such a reaction may be anticipated by preoperative intradermal testing with lens protein (antigen). The condition is to be avoided by using the intracapsular method of lens extraction in all cases of cataracts in which this technic is applicable. Avoidance of such a reaction is one of the strongest arguments in favor of this method. If the combined linear method of extraction is used, the anterior chamber must be cleared as thoroughly as possible of all residual lens material at the time of operation, either by expression or by irrigation. In cases of juvenile cataract the rapid method of eliminating the lens diminishes the possibility of the occurrence of such a reaction, but does not with certainty prevent it. Failure of operation in many cases of juvenile cataract is traceable to failure to consider the potential possibilities of absorption of lens protein in such cases. Precautionary measures may forestall such reactions—preliminary skin tests and preoperative desensitization with lens protein if indicated by the test; if the reaction occurs after cataract extraction or a needling operation, active hypsensitization with lens antigen is advised, usually in conjunction with a secondary operation to remove every vestige of lenticular matter.

With the advent of the plastic artificial eye, we have noted that a surprising number of persons who were wearing such eyes experienced abundant discharge from the socket, associated with discomfort and intense swelling and edema of the conjunctiva. The reaction subsides when the plastic eye is removed and is allowed to remain out of the socket for several days, but returns when the plastic eye is reinstated. Substitution of an old-fashioned glass eye does not cause reappearance of the reaction, but each time the plastic eye is inserted the reaction recurs, and the socket reassumes its former irritated state in a very

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13. Verhoeff, F. H., and Lemoine, A. N.: *Endophthalmitis Phacoanaphylatica*, Tr. Internat. Cong. Ophth., Washington 1922, pp. 234.

short time. This is cited as a form of atopism or allergy to the plastic material which ophthalmologists must be on guard to detect. Cytologic findings in the secretions in such cases have not been altogether consistent, nor have a sufficient number of cases been observed, and long enough, to justify a positive statement of the diagnostic value of the cytologic findings in the discharge in such reactions, but the indication is, most strongly, that certain of the plastics used in the manufacture of plastic eyes produce an allergic reaction, characterized by edema in the mucous membrane of the socket and a marked discharge. When such reactions occur, the offending prosthesis should be removed and the old-fashioned glass eye substituted, or another eye must be made from an entirely different plastic material, which, in turn, may or may not produce a reaction in the socket. Some patients may be sensitive to all types of plastic material but may be able to wear an old-fashioned glass eye with complete comfort and without any adverse reaction.

#### SUMMARY

Allergic reactions are of frequent occurrence in the eye and are of many kinds.

The etiologic factors are numerous.

Cytologic examination of the secretions from the eye is a definite aid in diagnosis in certain, but not in all, allergic conditions affecting the eye.

Attention is called to reactions in the eye caused by plastic prostheses, a condition which may be considered a form of atopism, or contact allergy.

323 Medical Arts Building.

## ANISOCORIA

### Attempted Induction by Unilateral Illumination

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THE VALUE of anisocoria as a diagnostic sign has been limited by reports of normal or physiologic anisocoria in as high as 40 per cent of all patients.<sup>1</sup> Löwenstein's pupillographic method has eliminated a large number of cases of these so-called physiologic anisocorias through detailed cinematographic analysis under both static and dynamic conditions.<sup>2</sup> In order to realize the potentialities of this method, and in order to place the proper value on the finding of anisocoria, it is necessary to delimit sharply that which may be physiologic from that which is pathologic. Toward this end the present study has been undertaken.

Several theories of the course of the afferent pupillary fibers have been proposed in attempts to explain various phenomena of the pupillary movements.<sup>3</sup> The most generally accepted schema is that proposed by Behr,<sup>3c</sup> who stated the belief that the macular fibers from each retina have equal representation in the constrictor nuclei of both sides, but that most of the extramacular fibers from each side are represented in the constrictor nucleus of the same side. That is, a greater number of extramacular fibers come from the nasal portion of the retina, cross in the chiasm and also decussate centrally. Magoun and Ranson<sup>4</sup> have shown the existence of a partial decussation of the pupillary paths in the posterior commissure. Whether such a decussation results in an unequal representation of extramacular fibers in the constrictor nuclei, as hypothesized by Behr, still lacks anatomic proof.

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From the Institute of Ophthalmology, Presbyterian Hospital, and the Department of Ophthalmology, Columbia University College of Physicians and Surgeons.

1. Walter: Ueber transitorische Pupillendifferenz bei Nervengesunden, *Neurol. Zentralbl.* **35**:619, 1916.

2. Lowenstein, O.: Pupillographic Studies: Present state of Pupillography; Its Method and Diagnostic Significance, *Arch. Ophth.* **27**:969 (May) 1942.

3. Bernheimer, S.: (a) Die Reflexbahn der Pupillarreaktion, *Arch. f. Ophth.* **47**:1, 1899. (b) Levinsohn, G.: Beiträge zur Physiologie des Pupillenreflexes, *Arch. f. Ophth.* **59**:436, 1904. (c) Behr: Die Lehre von den Pupillenbewegungen, Berlin, Julius Springer, 1924.

4. Magoun, H. W., and Ranson, S. W.: The Afferent Path of the Light Reflex. *Arch. Ophth.* **13**:862 (May) 1935.



Abelsdorff and Piper<sup>5</sup> reported anisocoria on unequal illumination of the eyes, the eye receiving the greater light having the smaller pupil. Their work was done with the illumination directed into the eyes along the visual axis in a manner similar to that used in the present study. Behr<sup>3c</sup> stated that the pupil of an eye blinded from a lesion of the retina or the optic nerve is larger than that of the seeing eye if the two halves of the retina of the seeing eye are equally illuminated. These two situations differ only in degree, since the blind eye may be likened to an eye in total darkness, with the fellow eye receiving light. From Behr's schema, the explanation of the phenomenon is as follows: The macular fibers have equal bilateral representation; most of the extramacular fibers of the brightly lighted eye cross in the chiasm, then cross again in the intercalated neuron, ending in the constrictor nucleus of the homolateral side; the remainder of the extramacular fibers of this eye do not cross in the chiasm but cross in the intercalated neuron to end in the constrictor nucleus of the opposite side; therefore, the constrictor nucleus of the homolateral side receives a stronger stimulus. Weiler, cited by Behr,<sup>3c</sup> was able to induce anisocoria as thus described in only 6 per cent of cases. However, the observations of Abelsdorff and Piper and others to the contrary, as well as Behr's explanation, have been carried over in more recent textbooks.<sup>6</sup> Only the most pertinent references are cited here. A fuller presentation of the literature has been given by Behr.<sup>3c</sup>

The present experiments attempt, under conditions of simulated unilateral blindness, to investigate the production of anisocoria as described in the preceding paragraph. Purely nasal or temporal illumination has been purposely avoided.

#### METHOD

Apparatus similar to that used by Löwenstein<sup>2</sup> was used in these experiments. A motion picture camera with double lenses recorded the pupils simultaneously side by side on 35 mm. film. The exposures were made at the rate of 10 per second. The film used was sensitive to infra-red rays and a basal infra-red illumination was maintained constantly on each eye. All experiments took place in a dark room.

The patients were adapted to darkness for fifteen minutes, after which pictures were taken to record the amount of anisocoria in darkness. Light reactions and psychosensory reflexes were performed and recorded to determine whether the responses for each patient fell within normal limits. The attempted induction of anisocoria was carried out as follows: A beam of blue-green light (Wratten filter XI), having a diameter of 4 cm. at the eye, was turned on the right eye

5. Abelsdorff, G., and Piper, H.: Vergleichende Messungen der Weite der direkt und der consensuell reagirenden Pupille, *Arch. f. Augenh.* **51**:366, 1905.

6. Spiegel, E. A., and Sommer, L.: *Neurology of the Eye, Ear, Nose, and Throat*, New York, Grune & Stratton, Inc., 1944.

from a distance of 33 cm. and at an angle 5 degrees above the visual axis; lateral displacement with regard to the visual axis was avoided; successive illuminations of 0.02, 12.0 and 92.0 foot candles were used; pictures were taken after six minutes' exposure to each of the first two intensities and after three minutes' exposure to the third intensity; the right eye was then returned to darkness, and the beam of the third (high) intensity was directed on the left eye for six minutes, and pictures were again taken.

## PRESENT STUDY

Twenty-five normal adult patients were examined, 9 of whom were males and 16 females. The anisocoria exhibited in darkness by these patients is shown in table 1. The average difference in darkness was 0.21 mm.

TABLE 1.—*Amount of Anisocoria in Darkness (25 Cases)*

Anisocoria (mm.).....	0.01- 0.10	0.11- 0.20	0.21- 0.30	0.31- 0.40	0.41- 0.50	0.51- 0.60	0.61- 0.70
Number of patients.....	8	4	6	3	3	0	1

TABLE 2.—*Changes in Anisocoria After Unilateral Illumination of Various Intensities*

	No Change	More Anisocoria	Less Anisocoria	Stimulated Pupil Relatively Larger	Stimulated Pupil Relatively Smaller
	A. Low Intensity (24 Cases)				
Number of patients.....	1	10	13	9	14
	B. Medium Intensity (25 Cases)				
Number of patients.....	0	13	12	9	16
	C. High Intensity (25 Cases)				
Number of patients.....	1	9	15	11	13

Table 2 A shows the changes found after six minutes' illumination of the right eye with dim light. The change in total anisocoria is less significant than the change of the stimulated pupil relative to its fellow. That is, a patient whose right pupil was larger in darkness might show decreased anisocoria after unilateral illumination of the right eye, indicating a relatively greater constriction of the stimulated pupil. On the other hand, if the left pupil had been larger in darkness, decreased anisocoria after illumination of the right eye would indicate a relatively greater constriction of the unstimulated pupil. In the 9 cases in which the stimulated pupil became relatively larger, the average increase was 0.15 mm. In the 14 cases in which the stimulated pupil became relatively smaller, the average decrease was 0.12 mm.

Table 2 B shows the changes found after six minutes' illumination of the right eye with light of medium intensity. There is little difference between these figures and those in part A of the table. In the 9 cases

in which the stimulated pupil became relatively larger, the average increase was 0.12 mm. In the 16 cases in which the stimulated pupil became relatively smaller, the average decrease was 0.12 mm. It should be noted that at the end of this series the stimulated eye had been under continuous illumination for twelve minutes.

Table 2 C shows the changes found after three minutes' illumination with the light of high intensity. At the conclusion of this series the eyes had been under light for fifteen minutes without interruption. In these results a lessened anisocoria in a significant number of patients is revealed. This may perhaps be explained as a function of the diminished size of the pupil under bright light. That is, an anisocoria which remains fairly constant in amount in the middle range of pupillary play decreases

TABLE 3.—*Changes in Anisocoria After High Intensity Illumination of the Opposite Eye (23 Cases)*

	No Change	More Anisocoria	Less Anisocoria	Stimulated Pupil Relatively Larger	Stimulated Pupil Relatively Smaller
Number of patients.....	0	8	15	9	14

TABLE 4.—*Analysis of Cases with Relatively Smaller Stimulated Pupil (57 Cases)*

Intensity	No. of Cases of Relatively Smaller Pupils	Per- centage of Total	Amount of Relative Constriction, Mm.						
			0.01- 0.10	0.11- 0.20	0.21- 0.30	0.31- 0.40	0.41- 0.50	0.51- 0.60	0.61- 0.90
Low (right).....	14	58	9	4	0	0	1	0	0
Medium (right).....	16	64	12	2	1	0	0	0	1
High (right).....	13	52	8	2	1	1	0	1	0
High (left).....	14	61	7	3	2	0	1	1	0

as the extremes of dilation or constriction are approached. Each iris may receive constrictor impulses in excess of the number needed for maximum constriction, so that the pupillary diameters may be very nearly the same, even though the imbalance of the constrictor impulses still exists. In the group of 11 relatively larger stimulated pupils, the average increase was 0.09 mm. In the 13 relatively smaller stimulated pupils, the average decrease was 0.15 mm.

Table 3 shows the changes after six minutes' illumination of the previously unlighted (left) eye with light of high intensity. It shows no essential differences from table 2 C and is susceptible of the same interpretation. In the 9 cases in which the stimulated pupil became relatively larger, the average increase was 0.14 mm. In the 14 cases in which the stimulated pupil became relatively smaller, the average decrease was 0.16 mm.

In table 4 the relative constriction of the stimulated pupils is analyzed for the whole series of cases. It shows that in 57 per cent of the cases the stimulated pupil constricted more, and more than half did so at every level of illumination. Of the 57 such instances, the relative constriction was less than 0.20 mm. in 47, or 82 per cent. This is less than the average anisocoria of 0.21 mm. exhibited in darkness by the whole series. If all the patients had shown no anisocoria in darkness, and if the same behavior on illumination had been shown, then a slight anisocoria, usually of less than 0.20 mm. would have developed in 57 per cent, with the lighted pupil smaller. Such was not the case. In this series an actual increase in anisocoria occurred in only 42 per cent, and in only 1 of these was the amount (0.88 mm., relative) grossly appreciable.

#### SUMMARY AND CONCLUSIONS

In a series of 25 cases attempts were made to induce anisocoria by unilateral illumination at three levels of intensity.

The average difference between the pupils in the dark-adapted patient was 0.21 mm. Only 1 subject showed an amount sufficient to be detected reliably by ordinary observation.

The change in the amount of anisocoria was approximately the same for all levels of illumination, namely, 0.02, 12 and 92 foot candles.

An actual increase in the amount of anisocoria was seen in 42 per cent of cases, while a relative increase, averaging 0.20 mm., was seen in 57 per cent. This apparently indicates a chance variation.

Contrary to the observations of Åbelsdorff and Piper<sup>5</sup> and the statements of Behr,<sup>3c</sup> the illuminated pupil did not constrict more than the unilluminated pupil. These results are similar to those of Weiler.<sup>3c</sup>

It appears that uniform illumination of one eye within the limits of time and intensity of this study may be disregarded as a cause of anisocoria. Since the technic of the experiments closely approximated that used by Löwenstein,<sup>2</sup> it follows that a factor of induced anisocoria is not inherent in his method.

It should again be emphasized that these studies were confined to illumination of the central portion of the retina and did not include stimulation of the temporal or nasal part of the retina.

Dr. Otto Löwenstein gave help and guidance in this study.

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## CEPHALOCELE OF POSTERIOR PART OF ORBIT

General Survey, with Report of a Case

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**B**Y CEPHALOCELE of the posterior part of the orbit is understood cerebral hernia arising from the middle cerebral fossa and penetrating into the posterior part of the orbit behind the bulbus oculi, through a preformed or nonpreformed opening in the wall of the orbit.

Posterior cephalocele of the orbit belongs to the group of basal cephaloceles. Besides the basal type, by far the rarest, there are occipital, frontal, parietal and lateral cephaloceles. Cephalocele of the anterior portion of the orbit, generally arising from the nasofrontal region, belongs to the frontal cephaloceles and is much more frequently observed than is the posterior lesion. Stadfeldt,<sup>1</sup> who was the first in Denmark to assess the available material, found in the literature up to 1902, 20 cases of anterior and 8 cases of posterior cephalocele. It has been the subject of some discussion whether a certain case (Oettinger's<sup>2</sup>) of the latter type should be counted as belonging to that group or be reckoned among the anterior cephaloceles. Schmidt,<sup>3</sup> who in 1927 reported a case, besides surveying available reports, did not include his tumor among the posterior cephaloceles. Nor is this case included in the present report, because, as first stated by Peters,<sup>4</sup> it appears from the description that the deficiency of the orbital wall was located so anteriorly that the lesion may reasonably be supposed to have originated from the nasofrontal area, and not, as asserted by Stadfeldt,<sup>1</sup> from the fossa media cranii.

Reali collected 140 cases of cephalocele, with the following distribution: occipital, 86 cases; frontal, 33 cases; parietal, 12 cases; lateral, 8 cases, and basal, 1 case. Estimates by Houel, Lawrence, Wallmann,

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1. Stadfeldt, A.: Ueber die Cephalocele der Augenhöhle, Nord. med. Arkiv., 1903, vol. 3, pt. 1, no. 12; vol. 4, no. 20.

2. Oettinger: Klin. Monatsbl. f. Augenh. 1874.

3. Schmidt, M.: On Multiple Cephaloceles in the Fossa Cranii Media, Acta psychiat. et neurol. 3:265, 1927.

4. Peters: Ueber einem Fall von doppeltseitiger Encephalocele der Orbita, Klin. Monatsbl. f. Augenh. 59:553, 1917.

and Larger and Lindfors are in agreement with Reali's distribution of favorite sites, whereas Deloff found the number of frontal cephaloceles to exceed the number of occipital cephaloceles.

Some dispute has arisen as to the term cephalocele, since the hernial content has not always consisted of cerebral tissue in cases with characteristic symptoms and in cases in which deformities of the bone, demonstrated by postmortem or by roentgenographic examination, were of the nature of hernial openings. Other designations have therefore been suggested and applied for short periods, the aim being a specification of the hernial content—meningocele, encephalocele, meningocephalocele, hydroencephalomeningocele and encephalocystomeningocele. The last designation was proposed by Muscatello, who stated the opinion that the condition was caused by cystic arachnitis, a view which he, among others, supported on the basis of microscopic changes in biopsy tissue of the cephalocele (epithelial proliferation, cystic degeneration and invasion of vessels).

In the present survey, comprising 31 cases of cephalocele of the posterior part of the orbit, only cases have been included in which the symptomatology was characteristic and in which roentgenologic or postmortem examination of the cranium established the presence of a hernial formation containing substance of the middle cerebral fossa and extending into the orbit behind the bulbus, either through a defect of the orbital wall or through an enlarged, preformed opening, as well as cases in which explorative operation of the orbit revealed tumors consisting of brain tissue—with or without membranes and with or without cystic degeneration—and cerebrospinal fluid.

In view of the comparatively high number of congenital cephaloceles and the frequency of unilateral deformities of bone in the form of incomplete ossification and the fact that in a single case only did meningeal symptoms precede the diagnosis of symptoms of cephalocele, it appears to me more reasonable to consider the cystic degenerative changes in the arachnoid (*a*) as secondary to the actual defect through which the hernial formation penetrates the orbit, and (*b*) as a natural consequence of the altered pressure and gradual compression which is associated with the hernial opening, similar to that which may be seen during operation for incipient incarcerated hernia. Nor does the fact that, of 8 patients who died after operation, degenerative, inflammatory changes of the meninges were observed in 7 support the view that this involvement of the meninges is the fundamental, primary disturbance. On the contrary, from the reports, it appears that in these 7 patients the meningeal symptoms appeared after operation, presumably as a consequence of exogenous infection (the cases in question are from a series of 14 operative cases, 5 of incisions, 7 of excisions and 2 of punctures).

The preformed openings through which cephalocele of the posterior portion of the orbit may penetrate are the optic foramen, the sphenoidal and sphenomaxillary fissures and the posterior ethmoidal foramen. They may be either of normal size or enlarged. In general, enlargements are unilateral, and they may affect all openings or one only.

The nonpreformed openings may be (a) congenital deficiencies (incomplete ossification, generally unilateral, or birth trauma), (b) traumatic defects of later origin or (c) defects caused by preexisting or concurrent disease. Listed in the order of their frequency, they are: erosion of bone due to aneurysms, malignant tumors, inflammatory processes, angiomas, generalized osteitis fibrosa cystica, osteitis deformans and internal hydrocephalus.

As a rule, the soft meninges and brain tissue form component parts of the hernial formation, whereas the dura mater is usually not involved in the later stages of the disorder but, bursting early in the development of the hernia, forms, together with the edges of the bone, part of the hernial opening. Only in the early stages, in which the lesion is not generally well developed yet is marked by symptoms characteristic of cephalocele of the posterior part of the orbit, does the dura mater form part of the hernial sac.

As a further sign that in by far the greater proportion of cases the primary disturbance is an abnormal development in early fetal life, the apparent existence of a gradual transition may be emphasized. It would appear likely that this transition starts in the manner exemplified in Borochovic's<sup>4a</sup> cases (1930): One of his patients, the fourth of 4 siblings, a girl aged 7, had double anophthalmos with orbital cyst, and her sister (sibling 3) had anophthalmos on the right side and microphthalmos on the left side, both patients having pronounced congenital defects of the roof, as well as of the posterior wall of the orbit. The transition might pass through the stage illustrated in the case described by Tauber in 1900 (with unilateral microphthalmos and incomplete ossification of the posterior wall, the roof and the floor of the orbit, so that the cranial cavity, the orbit and the maxillary sinus of the affected side formed a single cavity) to that in the case reported by Cohen,<sup>5</sup> with microphthalmos and enlargement of the optic foramen on the same side. It may further be emphasized that the microphthalmos which appears in 4 of the 31 cases collected here must be considered the result of abnormal development, like the cranial malformations, rather than as a secondary change consequent to the increased pressure in the orbit. Further, the disease is characterized, in most instances, by

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4a. Borochovic, S.: Kongeniter Anophthalmus mit Orbitalcyste, Ukrain. ophth. Ztschr. 3:122, 1930.

5. Cohen, M.: Orbital Meningo-Encephalocele Associated with Microphthalmia, J. A. M. A. 89:746 (Sept. 3) 1927.

being a congenital disorder, which may become manifest or aggravated as the result of trauma or the presence of an intercurrent disease. The condition progresses slowly. In isolated cases only does it manifest itself by serious symptoms, and rarely by general cerebral symptoms, such symptoms, when present, being epileptic fits, defective speech and impaired memory.

The material on which the present survey is based comprised 36 cases, reported as instances of cephalocele of the posterior orbit. From these must be eliminated 5 cases: (1) a case reported by Oettinger,<sup>2</sup> in which the possibility that the cephalocele originated in the anterior cranial fossa cannot with certainty be excluded, as, in addition to a deficiency corresponding to the ethmoid bone, the orbital plane was to all intents and purposes absent; (2) a case reported by Schousboe<sup>6</sup>; (3) a case reported by Kalt<sup>7</sup>; (4) a case reported by Tietze<sup>8</sup> before a German meeting of ophthalmologists in Munich in 1935, and (5) a case reported by Bonnet<sup>9</sup> in 1937. In the same year, however, Aronowich protested against the classification of Bonnet's<sup>9</sup> case with the cephaloceles, since it was clearly one of hernia of the dura mater. With respect to cases 2, 3 and 4, it may be said that the information available is too scanty to permit with certainty their inclusion in the group of cephaloceles of the posterior orbit. The remaining 31 cases were collected from the available literature published between 1841 and 1948. The cases concern 15 females and 9 males; for 7 patients there was no information as to sex. The ages of the patients at first examination ranged from 13 weeks to 77 years. By far the greater proportion were young persons: Twenty-two patients were under 30 and 3 over 30, while there is no statement as to the age of 6 patients. In 21 cases in which the patients were especially interrogated, there was no familial disposition to ocular diseases or congenital malformations. In 20 cases the condition had been accompanied with symptoms since shortly after birth, though to a comparatively slight degree. In 2 cases there had been serious trauma (Lücke and Tauber), pulsating exophthalmos quickly developing after a blow to the right eye in 1 case and blindness following head trauma, sustained at the age of 15 in the other. In the latter progressive symptoms of cephalocele of the posterior orbit had been present since birth, whereas in the former the patient had always been

6. Schousboe, F.: Méningo-encéphalocèle de l'angle supérointerne de l'orbite; excision; mort, Bull. Soc. d'opht. de Paris 1927, pp. 162-164.

7. Kalt, E.: Un cas d'encéphalocèle orbitaire, Bull. Soc. d'opht. de Paris, 1930, pp. 220-266.

8. Tietze, H.: Ein Fall von Meningoencephalocele der Orbita mit rudimentärem Augenanlage: Report, Gesellschaft für süddeutsch Augenärzte, München, 1935.

9. Bonnet, F.: Meningoencephalocele der Augenhöhle, *Semana méd.* 1:1025, 1937.



healthy up to the time of the accident and free from ocular disease. In 13 of 31 cases the initial examination revealed the tumor of the orbit, most frequently located medial to and passing behind the bulbus oculi. In all cases the tumors were soft, yielding and slightly elastic. In 20 cases the bulbus was displaced in relation to its original position in the orbit, being displaced downward and laterally in 18 cases and downward and medially (Wheeler<sup>10</sup> and Jaensch<sup>11</sup>) in only 2 cases. In Jaensch's<sup>11</sup> case there was, in addition to the anomalous posterior wall of the orbit, a defect in the lateral wall, through which the cephalocele had made its way. In 15 cases the mobility of the bulbus was limited.

In 28 cases there was unilateral exophthalmos, the condition being fairly equally distributed between the right and the left eye. In 26 cases exophthalmos was of pulsating type, the beats being of varied intensity and synchronous with the carotid pulse in all cases.

In 13 cases it was possible to correct the protrusion of the bulbus by slight pressure on the eyeball, resulting in simultaneous further protrusion of other contents of the orbit but without producing cerebral symptoms. In 3 cases attempts at reposition of the globe caused vertigo or nausea (Gala<sup>12</sup>; Schmidt and Jensen<sup>13</sup>; Strandberg). In no case did changes in the pulsation of the bulbus appear with the variation in the position of the head when the subject was in an upright position, while in 1 case Jaensch<sup>11</sup> reported considerable reduction in pulsation of the bulb after a prolonged period of quiet rest on the back. In 3 cases only was it possible to decrease the pulsation of the bulbus by compressing the carotid artery.

Kubli<sup>14</sup> mentioned aggravation of the pulsating exophthalmos on coughing, sneezing and forced contraction of the abdominal muscles, observations which correspond well with those of Gala to the effect that protrusion decreases in proportion to the quantity of cerebrospinal fluid withdrawn by lumbar puncture and that the cerebrospinal pressure increases when reposition of the protruding bulbus is attempted. Wheeler<sup>10</sup> observed that the pulsation of the eyeball disappeared and the protrusion diminished in the tribromoethanol anesthesia.

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10. Wheeler, J. M.: Pulsation of the Eyeball Associated with Defects in the Wall of the Orbit, *Bull. Neurol. Inst., New York* 5:476, 1936.

11. Jaensch, P. A.: (a) Encephalocele orbitae posterior, *Klin. Monatsbl. f. Augenh.* 76:433, 1926; (b) Encephalocele orbitae posterior, *Med. Klin.* 1:450, 1928; (c) Hydrocephalus congenitus und Cephalocele orbitae posterior, *Zentralbl. f. d. ges. Ophth.* 20:208, 1928; (d) Cephalocele orbitae posterior, *Klin. Monatsbl. f. Augenh.* 107:561, 1941.

12. Gala, A.: Encephalocele bei M. Recklinghausen, *Zentralbl. f. d. ges. Neurol. u. Psychiat.* 28:64, 1922.

13. Schmidt, L., and Jensen, F.: Un cas d'encéphalocèle postérieure d'orbite, *Arch. d'opht.* 39:108, 1922.

14. Kubli: Encephalocele unterm obern Lide, read before the Petersburg Ophthalmological Association, April 8, 1910.

Palpebral edema was present in 16 cases—the palpebra superior being involved in 13 cases and the palpebra inferior in 3 cases. Ptosis existed in 8 cases.

In 18 cases the size of the eyeballs was stated to have been normal, whereas in 4 cases microphthalmos (Taube, Delpuch,<sup>15</sup> Parson and Coates<sup>16</sup> and Cohen<sup>5</sup>) was present. Furthermore, in Cohen's case reduced tension and horizontal nystagmus were reported. In 7 cases the affected eyes had reduction of vision from 6/12 to total blindness. In 3 cases (Dandy,<sup>17</sup> Jaensch<sup>11</sup> and Wheeler<sup>10</sup>) diplopia was present, and examination showed changed visual fields in 2 cases (Dandy,<sup>17</sup> slight concentric contraction; Jaensch,<sup>11</sup> annular scotoma).

Ophthalmoscopic examination revealed changes in 5 cases. In 3 cases (Jaensch,<sup>11</sup> Dandy<sup>17</sup> and Stadfeldt<sup>1</sup>) there were overfilling and tortuosity of veins. In 1 case (Lagleyse<sup>18</sup>) papillary edges were blurred, and in 1 case (Parson and Coates<sup>16</sup>) there was coloboma of the optic nerve.

Among other ocular symptoms were interstitial keratitis, in 1 of Jaensch's cases; atrophy of the iris, cataract and stiff pupil, in 1 of Cohen's, and coloboma of the iris, in 1 of Stadfeldt's. In 2 cases there was audible vascular bruit, objectively demonstrated in 1 and subjectively felt in the other.

Cranial changes were many and characteristic: Enlargement of the orbit on the affected side, in 21 cases; visible asymmetry of the cranium, in 12 cases, and prominence of the temporal region, in 9 cases. In 4 of these 9 cases, in addition to posterior cephaloceles of the orbit, there was cephalocele of the temporal region (Jaensch,<sup>11a, d</sup> Schreyer and Sprenger<sup>19</sup> and Strandberg). Two of these cases deserve further mention. In the case published by Jaensch<sup>11a</sup> there was incipient cephalocele auricularis, examination at the ear clinic revealing a tense, pulsating prolapse of the dura mater in the external auditory canal. Schreyer and Sprenger's patient also had cephalocele auricularis, but the hernial opening of the cephalocele in the temporal region was not formed by suture edges or by deficiencies corresponding to a suture, as is usually seen, but by the temporal squama directly, in the middle of which the lesion was located.

In 7 cases there was enlargement of the optic foramen, and in 6 cases enlargement of the sphenoidal fissure, whereas the posterior

15. Delpuch, P. E.: *Traité des tumeurs de l'orbite*, Arch. d'opht., 1860.

16. Parson and Coates: A Case of Orbital Encephalocele with Unique Malformations of the Brain and Eye, *Brain* 39:108, 1906.

17. Dandy, W. E.: An Operative Treatment for Certain Cases of Meningocele (or Encephalocele) into the Orbit, *Arch. Ophth.* 2:123 (Aug.) 1929.

18. Lagleyse: *Arch. d'opht.*, 1900, cited by Stadfeldt.<sup>1</sup>

19. Schreyer, W., and Sprenger, W.: Ueber basale Cephalocelen, *Ztschr. f. Hals-, Nasen- u. Ohrenh.* 17:252, 1927.

ethmoidal foramen was enlarged and formed the hernial opening in only 1 case (Zitowskij <sup>20</sup>). In 12 cases there were palpable deficiencies in the orbital wall.

Roentgenographic or postmortem examinations in 15 cases revealed deficiencies in the orbital wall; these were located in the posterior wall in 8 cases, in the most posterior part of the roof in 4 cases, in the side wall in 3 cases (in the medial wall in 2 cases and in the lateral wall in 1 case (Jaensch <sup>11</sup>). In 2 cases the sella turcica was enlarged. Other defects causing cephaloceles of the posterior part of the orbit were the absence, in 5 cases, of the lesser wing and/or parts of the greater wing of the sphenoid bone (Jaensch <sup>11</sup> [1928 and 1941], Ecklentz,<sup>21</sup> Scullica <sup>22</sup> and Strandberg). In 2 cases there appeared, simultaneously, a cephalocele from the posterior cerebral fossa. In both cases the defect was located in the occiput (Jaensch <sup>11</sup> and van der Hoeve <sup>23</sup>). In 6 cases there were reported fistulas from the ventricular system to the cephalocele. The most serious defect was described in Tauber's case, with imperfect ossification of the lesser wing of the sphenoid bone, of the base of the greater wing of the sphenoid bone, of the cribriform plate of the ethmoid bone and of the upper and lower orbital walls.

The most frequent ocular symptom of cephalocele of the posterior part of the orbit is a slowly developing, unilateral exophthalmos, which appears chiefly in younger persons and, in the majority of cases, pulsates synchronously with the pulse and is reducible by pressure on the bulb, usually without accompanying cerebral symptoms but sometimes associated with vertigo and nausea. The exophthalmos may change in relation to the cerebrospinal pressure, whereas the pulsation in the majority of cases remains unaffected by compression of the carotid artery on the affected side. The eyeball is displaced, most frequently downward and laterally, but in few cases downward and medially if the deficiency is located in the lateral wall of the orbit. Movement of the eyeball is hampered, the degree being dependent on the size of the encephalocele. There is a palpable, soft, elastic tumor in the orbit. There is edema of the eyelids, most frequently of the upper and in some cases of the lower lid. Ptosis, reduced vision and microphthalmos must in all likelihood be regarded as due to defective development, in the same manner as are the skeletal deficiencies, rather than as secondary

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20. Zitowskij, M.: Zur Kasuistik der orbitalen cerebralen Hernien, *Sovet. vestnik. oftal.* 7:249, 1935.

21. Ecklentz: *Klin. Monatsbl. f. Augenh.*, 1901; cited by Stadfeldt.<sup>1</sup>

22. Scullica, F.: Esoftalmo da meningocele della fossa cranica media, *Ann. di ottal. e clin. ocul.* 2:734, 1927.

23. van der Hoeve, J.: Schädeldefekte bei Hydrocephalus, *Ophthalmologica Valencia* 1:237, 1935.

phenomena; further, there may be diplopia, central changes in the form of venous congestion, incipient papilledema and coloboma of the optic nerve, when the hernial opening of the cephalocele is formed by an enlarged optic foramen. In isolated cases there are changed visual field, bruit, reduced tension (observed only in cases with concurrent microphthalmos) and nystagmus.

#### OPERATIVE TREATMENT

Operative treatment was reported in 23 cases. In 3 cases ligation of the carotid artery on the affected side was done, with no improvement. In 5 cases incision of the palpable orbital tumor was carried out. In 7 cases incision of part of the hernial formation was performed (in 1 case, without ligation of the hernial sac). In 2 cases the sac was punctured. Of the cases, 14 in all, in which incision, excision or puncture was carried out, death was reported to have followed operation in 8. In 7 cases the cause was postoperative meningitis, and in 1 case, "cerebral crisis." In 4 cases transplantation was carried out with living tissue. In 1 case trepanation was done, with dural substitute, and in 1, craniotomy, with use of gel film. In the last-mentioned 6 cases the patients survived, and the symptoms were noted to improve; the bone healed well in the 4 cases of transplantation.

Although the number of operations carried out is small and the descriptions in several cases are incomplete, the results indicate that patients are best served by operations similar to those for hernial lesions; i. e., craniotomy, reposition of the contents of the hernia and substitution according to the defect—bone transplantation in smaller defects; gel film, of a thickness suitable to the size of the defect, in larger ones, or dural substitute, if and when practicable.

#### REPORT OF CASE

A case of cephalocele of the posterior portion of the orbit from the University Hospital, Copenhagen, is reported.

A girl aged 6 had a condition diagnosed as pulsating exophthalmos and was referred to the ophthalmologic department of the hospital on Feb. 23, 1948.

She had had the usual diseases of childhood without complications. There was no familial disposition to ocular disease or congenital malformations. She was the last of 4 siblings. She had previously been in good health, and her mental and physical development corresponded to the normal for her age.

The present disorder had been observed by her mother during the last year; it manifested itself by pulsation of the right eye in the orbit, synchronous with the pulse, as well as increasing asymmetry of the cranium, with thickening of the right temporal region. No other abnormalities were observed by her mother.

*Physical Examination.*—The child was apparently normal and healthy. Physical and mental development was normal for her age. Stethoscopic examination showed a normal condition of the heart and lungs. The abdomen was soft and normal; there were no neurologic abnormalities.

**Cranium:** There was slight asymmetry of the face. The right temporal region showed a watch glass-shaped prominence. Corresponding to and along the sphenoparietal suture was felt a cranial defect, 3 to 5 mm. broad and just under 2 cm. long. No hernial formation was felt there, but pressure elicited a soft, elastic resistant mass, and the area was only slightly tender.

**Ocular Examination.**—Vision was  $3/4.5$  in each eye, without correction.

The right orbit was larger and more ovoid than the left. No palpable deficiency of the orbital wall was noted. There was slight protrusion of the right eyeball, which pulsated synchronously with the pulse, with varying magnitude, the maximum pulse being 3 mm. and the minimum scarcely visible. Neither the protrusion nor the pulsation was altered by rotation of the head. During repeated attempts to compress the carotid artery of the affected side, it appeared once as though the pulsation of the eyeball was decreasing; it returned, however, before the compression was discontinued.



Fig. 1.—A girl aged 6 with cephalocele of the posterior part of the right orbit. *A* shows symmetry of the face, with prominence of the right temporal region and the right eyeball in a more lateral and downward position than the left. *B*, patient seen from the side at an oblique angle, showing prominence of the lower frontal part of the right temporal region.

Exophthalmometric measurements (Hertel) were 15 mm. on the right side and 13 mm. on the left side. The protrusion could be reduced by pressure, thereby causing slight prolapse of the content of the upper portion of the orbit, accompanied with a slight feeling of discomfort, slight nausea and uncharacteristic vertigo.

No bruit was audible on auscultation of the cranium. There was no nystagmus or double vision. The right bulbous could be moved freely in all directions, to the same extent as the left eye. The right eyeball was displaced slightly downward and laterally. There was no strabismus. The cornea, conjunctiva, anterior chamber, lens and iris were normal in each eye.

Ophthalmoscopic examination revealed a normal condition on both sides.

**Roentgenographic Examination** (Dr. Gilg).—The cranium was normal in shape and size. The sella turcica was normal. The left orbit was normal, whereas the right orbit was a little larger and more ovoid; corresponding to the

entire background of the orbit was a large defect, the upper edge of which was clearly discernible, whereas its lower limit was difficult to locate. The defect seemed to affect great proportions of the wings of the sphenoid bone. No signs of defect appeared elsewhere in the cranium. The paranasal sinuses were weakly developed.



Fig. 2.—*A*, roentgenogram of the cranium in the frontal plane. The right orbit is larger and more ovoid than the left. There is no sphenoidal fissure on the right side or visible posterior wall of the right orbit. *B*, roentgenogram taken in the right lateral position. The right sphenoidal wing is strongly dislocated upward and lies like an arc over the right orbit.

Roentgenographic examination (Prof. F. Møller) of the cranium in the frontal plane repeated nine days later showed that the right orbit was larger and more ovoid than the left. Here it was not possible to see the posterior wall or the sphenoidal fissure, and the wings of the sphenoid bone appeared to be displaced upward to a considerable degree, lying like an arc over the upper part of the orbit. The same phenomenon was noted on special exposure of the optic foramen, which in itself presented no abnormalities. A roentgenogram in the right lateral position revealed the same displacement, and one received the impression that pressure was being exerted by an unknown factor, which had produced the dislocation and caused erosion of the posterior lateral wall of the orbit. No abnormalities of the paranasal sinuses could be demonstrated, but the frontal ethmoidal sinuses were very incompletely developed.

Planigrams of the right orbit were then attempted, but the pictures were not so valuable as they might have been because the patient moved during exposures.

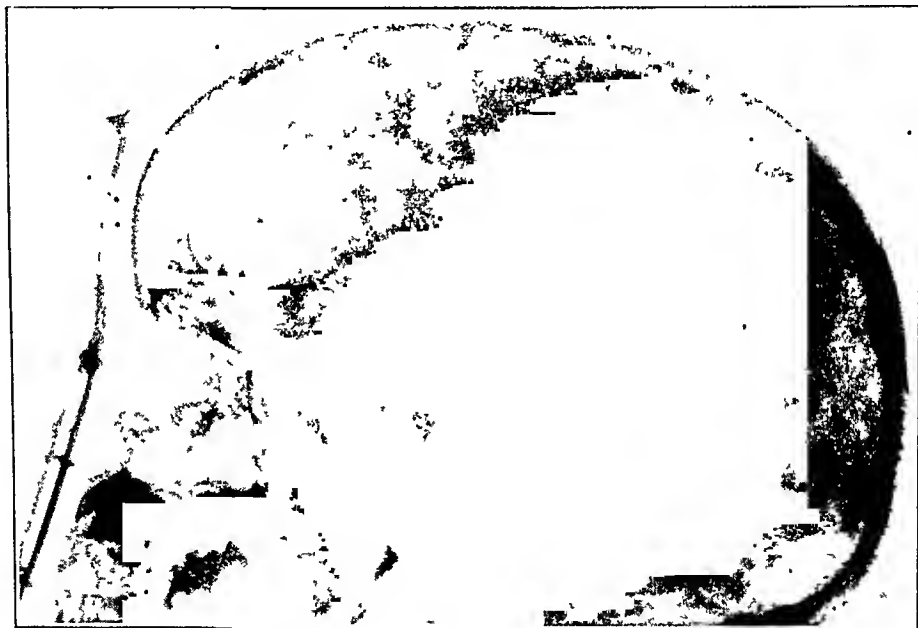


Fig. 3.—Arteriogram of the right side, showing compression of the carotid sinus on the right side. There is no sign of aneurysm.

March 19, 1948: The patient was moved to the neurosurgical department of the University Hospital for arteriography and possible operation. Here, ophthalmologic and neurologic examinations gave the results previously noted.

March 22: Arteriograms (Prof. Busch) revealed a peculiar prominence of the carotid siphon on the right side, which may have been produced by the examination, but the presence of partial carotid block was beyond doubt.

March 23: A ventriculographic examination was performed. The fluid pressure was 140 systolic and 100 diastolic. Roentgenograms showed no abnormalities. Operation was decided on and was performed by Prof. E. Busch.

*Operation.*—A frontal cutaneous incision was made over the anterior part of the right hemisphere. The tumor of the temporal region appeared to be only a blister in the bone over a strongly protruding temporal lobe. The wing of

the sphenoid bone was in an extreme frontal location, only 2 cm. from the orbital process, and followed the middle meningeal artery, which was about 2 mm. thick. The fissure of Sylvius was very deep, whereas the bone itself, especially the wing of the sphenoid bone, was as thin as paper. It was removed laterally by forceps and the dura mater was opened. It was then possible to penetrate to the middle fossa and to the posterior wall of the orbit, where it appeared that no bone had formed; only a thin, incomplete membrane of connective tissue separated the middle fossa, corresponding to the temporal pole, from the orbital contents. Exploration was carried through the frontal lobe to the internal carotid artery, which was peculiarly twisted in relation to the dura mater, but there were no signs of tumor or aneurysm. The posterior wall of the orbit was covered with a gel film, and the dura was completely sutured. The wound was closed after the piece of bone on the temporal side had been slightly reduced.

*Postoperative Course.*—The patient stood the operation well. The post-operative course was uncomplicated.

On March 30 the patient was moved back to the ophthalmologic department; she felt entirely well. A faint pulsating exophthalmos was still present, though to a considerably less pronounced degree. Dislocation of the eyeball was decreasing. The patient was discharged on April 16, to report at intervals for continued control.

#### SUMMARY

On the basis of 31 cases of cephalocele of the posterior part of the orbit collected from the literature between 1841 and 1948, the most prominent pathologicoanatomic changes are reviewed. Various reasons are cited in support of the concept that this lesion is a congenital malformation, caused by failure in ossification, rather than a condition following cystic degenerative arachnitis, a view previously held. Directions for treatment are given. In conclusion, a recently diagnosed Danish case is reported.

Prof. H. Ehlers, M.D., drew my attention to this case and encouraged me in the writing of the present report.

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## GONIOTOMY IN TREATMENT OF CONGENITAL GLAUCOMA

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THE RESULTS obtained from goniotomy in the treatment of 16 eyes (9 patients) with congenital glaucoma are reported. The outcome in these eyes is comparable to the reported by Barkan.<sup>1</sup> All the patients discussed in this paper have been followed for one and one-half to three years after operation.

### HISTORICAL REVIEW

The treatment of congenital glaucoma has been discouraging in the past. Favorable response to miotics is rare. The multiplicity of operations in use in the various clinics speaks for their inadequacy. Anderson,<sup>2</sup> in his monograph, pointed out that congenital glaucoma is one of the chief causes of blindness in children. He cited surveys from several countries which showed that 2.4 to 13.5 per cent of children admitted to schools for the blind had lost their eyesight because of congenital glaucoma. He concluded his monograph by dwelling on the poor outlook for patients with congenital glaucoma and stated that there is little hope of preserving vision sufficient for earning a livelihood.

The excellent results from goniotomy reported by Barkan afforded a striking contrast. Incision of the angle of the anterior chamber for the treatment of congenital glaucoma was first reported by de Vincentiis in 1893.<sup>3</sup> Anderson<sup>4</sup> stated that several Italian and French ophthalmic surgeons have since used the operation in the treatment of congenital glaucoma. Some good results were apparently obtained, but the operation has never become popular or widely used.

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Read at the Eighty-Fifth Annual Meeting of the American Ophthalmological Society, Hot Springs, Va., June 2, 1949.

From the Department of Ophthalmology, Hospital of the University of Pennsylvania and University of Pennsylvania School of Medicine.

1. Barkan, Otto: (a) Operation for Congenital Glaucoma, *Am. J. Ophth.* **25**:552-568 (May) 1942; (b) *Technic of Goniotomy for Congenital Glaucoma*, *Tr. Am. Acad. Ophth.* **52**:210-226 (Jan.-Feb.) 1948.

2. Anderson, J. R.: *Hydrophthalmia, or Congenital Glaucoma*, London, Cambridge University Press, 1939, pp. 4 and 5.

3. de Vincentiis, C.: *Incisione dell'angolo irideo nel glaucoma*, *Ann. di ottal.* **22**:540, 1893.

4. Anderson,<sup>2</sup> p. 312.

Barkan used the procedure on 17 eyes and first reported his results in 1942.<sup>1a</sup> The tension was normalized in 16 of the 17 eyes, and visual function was maintained in 14. In 2 of the 3 blind eyes, vision had been lost before surgical treatment was instituted. In only 1 eye, therefore, did operation fail to normalize the tension in time to save vision. In 1947,<sup>1b</sup> Barkan added the results obtained in 76 eyes with congenital glaucoma. In 66 of these the tension was normalized and vision maintained. All of the children had been followed from one to ten years. He concluded that the operation if performed early gave excellent results. He, therefore, made a plea for early diagnosis and prompt surgical intervention.

The results obtained in the treatment of congenital glaucoma at the Hospital of the University of Pennsylvania over a period of years had been highly disheartening. Because of these discouraging results and in view of Barkan's reports, my colleagues and I decided to try goniotomy, using it first in June 1946 on 2 eyes nearly blind from the disease (cases 1 and 2). The tension was not controlled, but since the operation seemed relatively safe we used it in more normal eyes.

#### TECHNIC

Operation was done with the patient under ether anesthesia. A Barkan knife<sup>®</sup> was used without aid of the goniotomy lens. We attempted to use the lens in the operation on 2 eyes, but it was cumbersome and contact with the cornea was difficult to maintain. The goniotomy knife was swept along from one-third to one-half the circumference of the eye, which was as much as could be reached at each operation. Miotics were used after operation in some eyes but seemed to have no effect on the outcome. Postoperative gonioscopy demonstrated scattered peripheral anterior synechias along the incised portion of the angle of a few eyes. More recently, therefore, we have filled the anterior chamber with air after goniotomy, employing the method outlined by Chandler.<sup>5</sup> An oblique incision is made with a knife needle in the lower temporal portion of the cornea through which air can be introduced with a fine needle, the tip of which not only enters the tract but goes through into the anterior chamber. All of our patients were reexamined at intervals of six weeks to three months during the first year after operation and then at least every six months. All tensions were recorded with the patient under general anesthesia.

#### PRESENTATION OF CASES

CASE 1.—H. W. B., a 21 month old white boy, was admitted to the ophthalmologic clinic of the Hospital of the University of Pennsylvania on June 6, 1946. When he was 6 months of age, his pediatrician had first noticed that his eyes appeared abnormally large and referred him to an ophthalmologist for care. From that time until he was 21 months of age, a fifteen month period, seven paracenteses were performed on his right eye, the last in March 1946, and three on the left eye, the last in February 1946. The parents stated the belief that

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5. Chandler, P. A.: Symposium Primary Glaucoma: V. Complications of Surgery, *Tr. Am. Acad. Ophth.* **53**:224-231 (Jan.-Feb.) 1949.

vision was poor in his right eye but that he could see well with his left eye. There was no family history of similar illness. He was a full term child. His mother had had no illness during her pregnancy. The child had always been healthy, and his development had been normal except for his eyes.

General physical examination revealed nothing remarkable. No other congenital anomalies were found. The reaction to a Kahn test was negative.

*Examination of Eyes.*—Visual Acuity: The child followed objects with the left eye only.

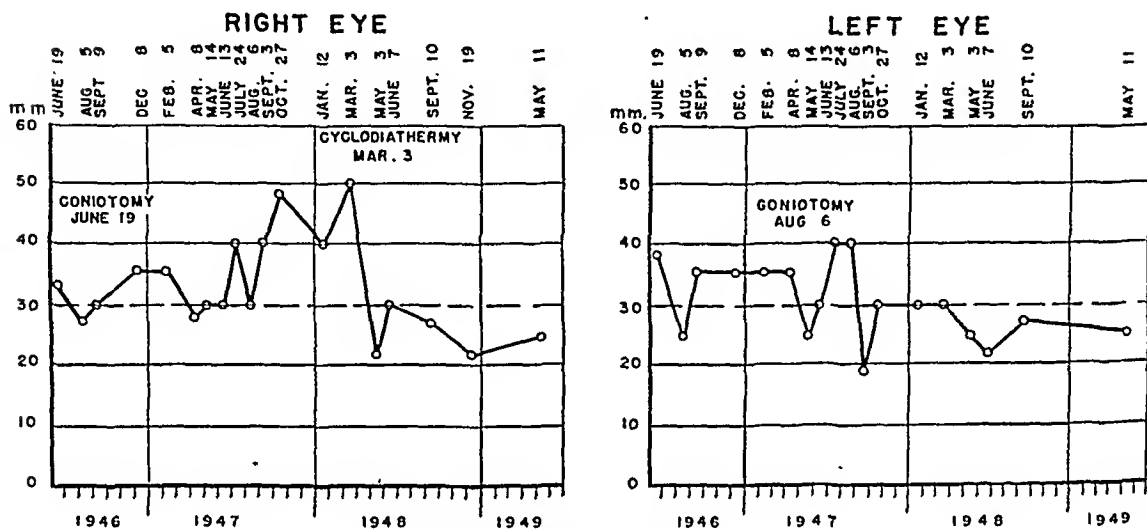


Fig. 1.—Tensions in case 1.

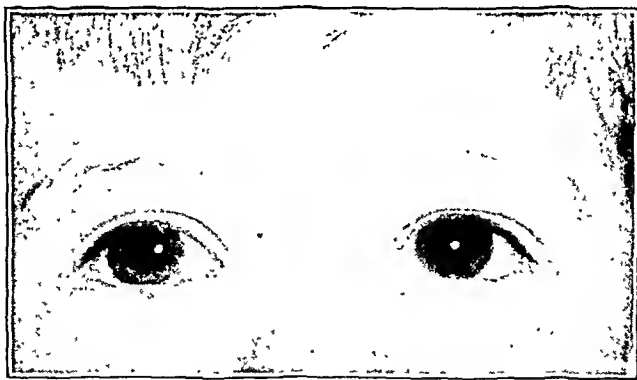


Fig. 2 (case 1).—Photograph taken at 4½ years of age, three years after goniotomy on the right eye, one year after cyclodiathermy on the right eye and approximately two and one-half years after goniotomy on the left eye.

*External Examination:* The lids were normal. Both palpebral fissures were somewhat widened. The corneas were definitely enlarged, the right more so than the left. Both corneas appeared clear to the naked eye. The anterior chambers were deep. The eyes were white. The right pupil reacted sluggishly to direct light; the left, normally.

*Ophthalmoscopic Examination:* Right eye: The media were clear except for lines in Descemet's membrane. The optic nerve was pale and deeply cupped. The retinal vessels were normal. The macula was healthy.

Left eye: This eye was similar to the right eye except that the optic nerve head was normal.

Ocular Tension: Tension was 33 mm. of mercury in the right eye and 38 mm. in the left eye (with a 7.5 Gm. weight and with the Schiøtz tonometer).

Gonioscopic Examination: Translucent embryonic tissue in the angle of the anterior chamber apparently displacing the iris toward the wall of the angle could be seen in each eye.

Impression: The impression was bilateral congenital glaucoma. Defective vision in the right eye was due to optic nerve atrophy.

*Subsequent Clinical Course.*—The child was admitted to the Hospital of the University of Pennsylvania for treatment. Because of Barkan's remarkable results with goniotomy, we elected to carry out this procedure on the right eye. Having had no experience with the procedure, we chose to do it on this eye, which was the patient's poorer one, having only questionable vision. Goniotomy was therefore performed, with the use of ether anesthesia, on June 19, 1946, without mishap. The eye showed little reaction. The child was discharged from the hospital two days later, to be observed subsequently in the outpatient department. The next ocular tension recorded was on Aug. 5, 1946, when it was 27 mm. of mercury in the eye operated on and 25 mm. in the left eye. Measurements of tension were made at regular intervals of about two months during the next year (fig. 1). The ocular tension in the surgically treated eye varied during that time from 27 to 40 mm. of mercury. The tension in the left eye was somewhat lower until July and August 1947, when it was recorded at 40 mm. of mercury on two successive occasions. The cornea was increasingly hazy.

By this time we had obtained apparently excellent results from goniotomy in several other patients with congenital glaucoma. We therefore recommended this procedure for his left eye, and the operation was performed on Aug. 6, 1947. Slight bleeding into the anterior chamber occurred, but the hemorrhage absorbed promptly and convalescence was uneventful. The tension of the left eye has since remained normal. The tension in the right eye, however, gradually rose until in March 1948 it was 50 mm. of mercury. In an attempt to save the eye, a cyclodiathermy was performed on March 3; since this time the tension has been stabilized at 22 to 30 mm. of mercury. Both corneas are at present clear (fig. 2).

*Results of Goniotomy.*—In the right eye, goniotomy failed, probably due to the advanced state of the disease, and cyclodiathermy subsequently normalized the ocular tension. In the left eye, tension was controlled by goniotomy.

CASE 2.—A. O. K., a 12 year old white boy, was first admitted to the ophthalmologic clinic of the Hospital of the University of Pennsylvania on May 20, 1946, because of poor vision in his left eye. This had first been observed four months previously during a routine examination of the eyes by the school physician. He also had had some discomfort in the eye. His right eye had always seemed normal. No history of previous ocular difficulty could be obtained. He had had measles at 5 years and mumps at 7 years of age. No family history of ocular disease could be elicited. The results of general physical examination were not remarkable.

*Examination of Eyes.*—Visual Acuity: Vision was 6/9 in the right eye and was limited to hand movements in the left eye.

**External Examination:** The eyelids were normal. The left palpebral fissure was slightly wider than the right, and the left eyeball was somewhat more prominent than the right. Both corneas were slightly large, the left, measuring 14 mm., being larger than the right (13 mm.). To the naked eye they appeared clear. Ocular rotations were full. The conjunctiva and sclera appeared healthy. The pupils were round and regular, but the left (5 mm.) was larger than the right (4 mm.). Both reacted promptly in convergence. The right pupil reacted promptly to direct light but poorly to indirect light. The left pupil reacted in the opposite manner, a response characteristic of damage to the left optic nerve.

**Examination with Slit Lamp:** The corneas were clear except for ruptures of Descemet's membrane in each eye.

**Ophthalmoscopic Examination:** Right eye. The disk was normal in color and outline. The physiologic cup was normal in size and depth. The retinal vessels were normal. The macula was healthy. No lesions could be seen.

Left eye. The findings were similar to those in the right eye except that the disk was very pale. A large glaucomatous cup was present, extending to the margin of the disk. The vessels dropped sharply over the edge. Arterial pulsation was seen at the edge of the cup.

**Ocular Tension:** Tension was 22 mm. (5.5 Gm. weight) in the right eye and 35 mm. in the left eye (7.5 Gm. weight).

**Visual Fields:** Right eye. The peripheral field was full to a 1/330 white test object, and the central field was full to a 1/1,000 white test object. The blindspot was normal. No scotoma could be elicited.

Left eye. Only a residual temporal field to light remained.

**Impression:** The impression was that of (1) congenital glaucoma, with spontaneous cure in the right eye, and congenital glaucoma, with optic nerve atrophy in the left eye.

**Subsequent Clinical Course.**—Pilocarpine nitrate, 1 per cent, and physostigmine salicylate, 0.5 per cent, were prescribed four times daily for the left eye, but this medication failed to reduce the tension, which continued to be between 36 and 42 mm. of mercury during the following week. DFP (di-isopropyl fluorophosphate), 0.1 per cent, once daily likewise failed, although extreme miosis resulted.

The child was therefore admitted to the hospital, where a goniotomy was performed on his left eye on June 21. A considerable hyphema occurred, which absorbed promptly. Tension at the time of his discharge from the hospital was 22 mm. of mercury in the eye operated on. The tension of the eye was never over 22 mm. of mercury.

After his discharge from the hospital, the tension in the left eye remained normal for only a short time. On August 5, it was found to be 35 mm. of mercury and subsequently has never been below 40 mm., and has been as high as 65 mm. of mercury. The goniotomy was judged a complete failure. The tension in the right eye has fluctuated between 17 and 22 mm. of mercury, apparently representing spontaneous recovery from congenital glaucoma.

**Results of Goniotomy.**—Goniotomy produced spontaneous cure in the right eye and failed to relieve the glaucoma in the left eye, probably owing to the advanced state of the disease.

**CASE 3.**—T. B., a 9½ month old white boy, was admitted to the ophthalmologic clinic, Hospital of the University of Pennsylvania, on March 19, 1946. His eyes had been large since birth, and he had always been extremely sensitive to light.

He was seen by an ophthalmologist when only a few days old and pilocarpine was prescribed. His eyes continued to become larger, however, and the sensitivity to light increased. His parents believed that his vision was very defective.

His delivery had been normal at full term. He had had no illnesses. His development was normal. His mother had been healthy throughout her pregnancy. There was no family history of ocular disease. The results of general physical examination were not remarkable. The reaction to a Kahn test was negative.

*Examination of Eyes.*—Visual Acuity: The patient followed a light with each eye.

*External Examination:* The eyelids were normal. Both corneas were greatly enlarged, measuring 14 mm. in diameter. The anterior chambers were deep. Each cornea was diffusely cloudy. Iridodonesis was seen in each eye. The pupils reacted to light. The conjunctivas were slightly injected. The scleras had a somewhat bluish appearance.

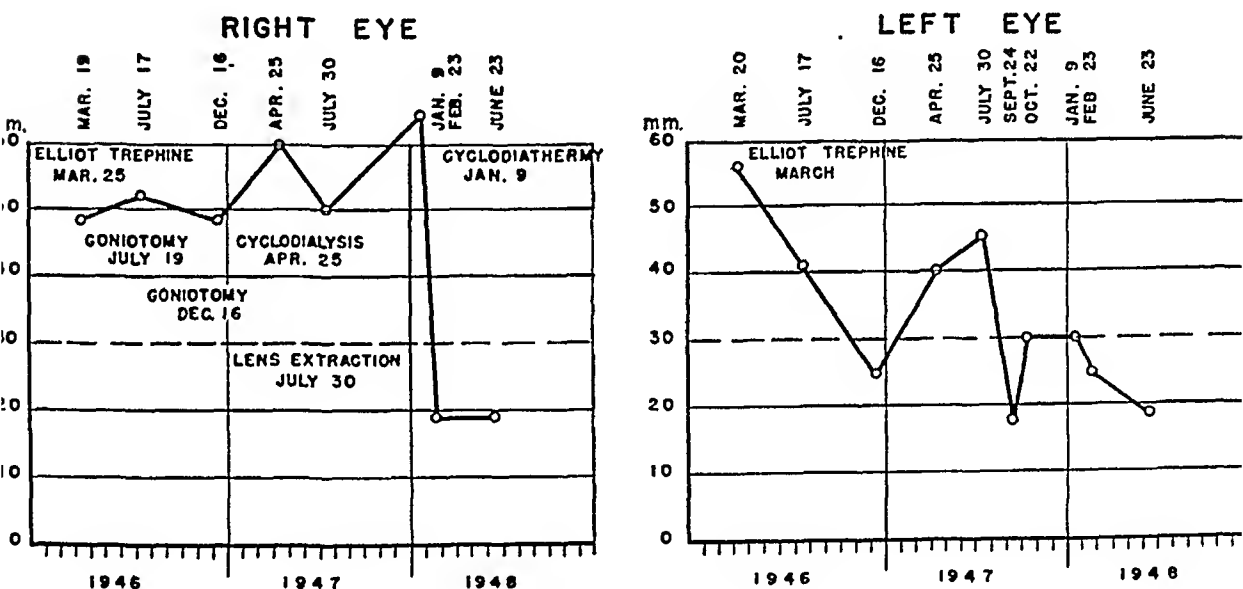


Fig. 3.—Tensions in case 3.

*Examination with Slit Lamp:* Ruptures of Descemet's membrane were present in each eye.

*Gonioscopic Examination:* The angles could not be seen because of a corneal haze.

*Ophthalmoscopic Examination:* A view of the fundus was also prevented by corneal opacity.

*Ocular Tension:* Tension was 48 mm. of mercury in the right eye and 56 mm. in the left eye (7.5 Gm. weight).

*Impression:* The diagnosis was bilateral congenital glaucoma.

*Subsequent Clinical Course.*—He was admitted to the Hospital of the University of Pennsylvania on March 19 for further treatment. At that time we were not yet doing goniotomies; so a bilateral Elliot trephination was done. Operation was performed on the right eye March 25 and on the left eye on March 29. The procedure was uneventful in the right eye, although the limbal tissue was found to be extremely thin. However, in the left eye vitreous presented in the trephine opening after the iridectomy. Persistent iridocyclitis developed in this eye,

and the cornea became opaque. The patient was discharged from the hospital two weeks later. A filtering bleb failed to develop in either eye. The tension was only temporarily lowered. He was subsequently followed in the outpatient department where the tension was found to rise gradually, until in July tension in the right eye was 52 mm. of mercury (7.5 Gm. weight) and that in the left, 40 mm. (fig. 3). The cornea of the left eye had become permanently opaque. He was readmitted to the hospital on July 19, 1946, because of the elevated tension, and a goniotomy was done on the right eye. A rather severe hyphema complicated the operation, but this absorbed during the next three weeks. He was again followed in the outpatient department, but the tension again gradually rose until it was 48 mm. of mercury on Dec. 16, 1946. Another goniotomy was done on the right eye, which was again accompanied with hyphema, which absorbed slowly. The tension was again lowered, but for only a short time, after which it again rose, this time to 60 mm. of mercury. We felt that his eye was probably too degenerated to be treated by goniotomy and, in desperation, resorted to cyclo-dialysis, on April 25. Severe hemorrhage in the anterior chamber ensued. The eye was then so badly damaged by the glaucoma and previous surgical procedures that the hemorrhage persisted two months. When absorption had taken place, it was observed that the lens in this eye was subluxated. Because the tension continued at 50 to 60 mm. of mercury, the lens was removed, with the thought that it might be contributing to the elevated tension. Extraction was accomplished successfully, without loss of vitreous, on July 30, 1947.

This procedure likewise failed to control the tension of the right eye, which was 64 mm. of mercury on Jan. 9, 1948. Because the child was having considerable pain and the parents wanted everything possible done to retain the eye and the light perception, which was still present, cyclodiathermy was carried out. Since then, the tension in his right eye has been within normal limits. The left eye gradually became phthisical.

*Result.*—The left eye was blind and phthisical, after the Elliot trephination; the right eye had light perception; goniotomy failed as secondary procedure in this eye.

*CASE 4.*—N. S., a four month old boy, was seen through the courtesy of Dr. Francis Heed Adler, on March 28, 1946. The child had been photophobic from birth. His parents had noticed that his corneas had become cloudy during the preceding month. He had been born at full term, after an uneventful pregnancy. His development had been normal. There was no history of blindness in his family. The results of general examination were not remarkable. The reaction to a Kahn test was negative.

*Examination of Eyes.*—Visual Acuity: The infant was attracted by moving objects before either eye.

*External Examination:* The eyelids were normal. The palpebral fissures were slightly widened. Ocular motility was normal. Each cornea was enlarged, the right being about 13 mm. and the left 14 mm. in diameter. Photophobia was severe. The pupillary reactions to light were intact. The conjunctivas were hyperemic, but there was no discharge.

*Examination with Slit Lamp:* Both corneas were hazy. Ruptures of Descemet's membrane were present in each eye.

*Ophthalmoscopic Examination:* This examination could not be made because of the clouding of the corneas.

Ocular Tension: Tension was 38 mm. of mercury in the right eye and 35 mm. of mercury in the left eye (7.5 Gm. weight).

Impression: The diagnosis was bilateral congenital glaucoma.

*Subsequent Clinical Course.*—Bilateral Elliot corneoscleral trephination was done during the two weeks subsequent to his admission. At that time we had not as yet employed goniotomy in the treatment of congenital glaucoma. No operative complications were encountered, and convalescence was uneventful. Miotics were employed after operation, and the patient was reexamined at frequent intervals. Filtering blebs did not develop, and the tension of each eye was only temporarily controlled. On May 20 it was found to be 40 mm. of mercury in each eye (fig. 4). Both corneas were again cloudy and edematous. During June and July the cloudiness of the cornea continued and the tension as determined by palpation remained elevated in each eye.

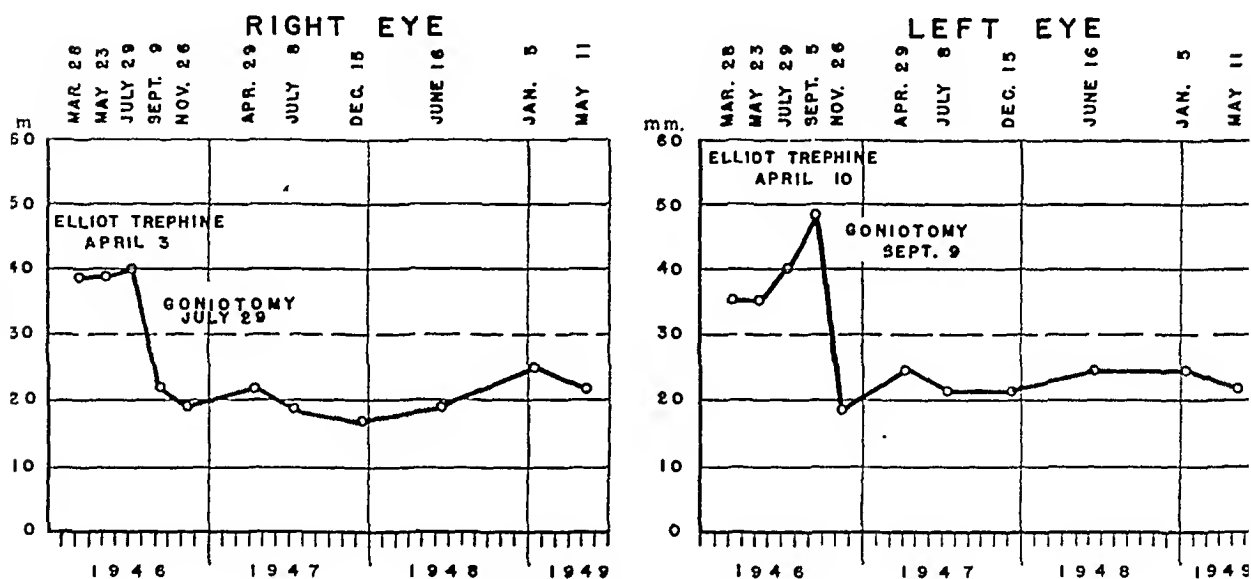


Fig. 4.—Tensions in case 4.

On July 29, therefore, a goniotomy was done on the right eye. Operation and convalescence were uneventful. Pronounced improvement in the eye resulted. The cornea of the treated eye cleared, but the intact (left) eye remained cloudy during the following six weeks. Because of the seemingly excellent result in the right eye, a goniotomy was performed on the left eye on September 9. The procedure was again carried out without complication. The child was seen at three month intervals after this operation until December 1947. Since then the intervals have been increased to six months. During this time the tension has been recorded as between 17 and 30 mm. of mercury. The corneas have remained clear.

After the goniotomies, ophthalmoscopic examination was easily carried out. The fundi were found to be very myopic, being seen with a  $-11.00$  lens on each side. The disks were large. No glaucomatous cup or atrophy was present.

Postoperative gonioscopic examination revealed peripheral anterior synechias at the site of the goniotomy in the right eye. None were seen in the left eye. The child seems to have normal visual function except for high myopia (fig. 5).

Result.—Tension was controlled by bilateral goniotomy after corneoscleral trephination had failed.



CASE 5.—J. M., a 4 month old boy, was admitted to the ophthalmologic clinic of the Hospital of the University of Pennsylvania on Nov. 19, 1946. At birth his eyes were observed to be larger than normal, and he was sensitive to light. One week before he was brought to this clinic each cornea had become cloudy. His birth had been spontaneous, following a full term, uncomplicated pregnancy. Postnatal development had been normal. There was no history of ocular trouble or of blindness in the family. The general physical examinations revealed nothing remarkable. The reaction to a Kahn test was negative.

*Examination of Eyes.*—External Examination: The eyelids were normal. Ocular motility seemed full. Both corneas were enlarged, each being 13 mm. in diameter and definitely cloudy. The pupils reacted to light. The conjunctiva and sclera were healthy.

Gonioscopic Examination: The corneas were too cloudy to permit visualization of the angles.

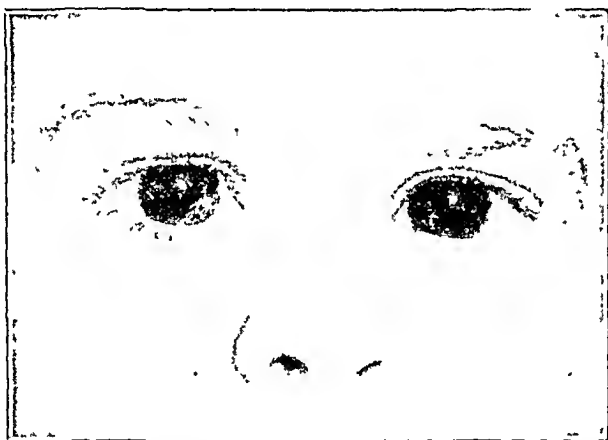


Fig. 5 (case 4).—Photograph taken at  $3\frac{1}{2}$  years of age, two years and eight months after goniotomy on the right eye and two years and six months after goniotomy on the left eye.

Ophthalmoscopic Examination: Although fundus detail was difficult to see because of corneal haziness, the right disk appeared normal. The left nerve head seemed suspiciously cupped. The color of each disk was good.

Ocular Tension: Tension was 40 mm. of mercury in the right eye and 35 mm. of mercury in the left eye (7.5 Gm. weight).

Impression: The impression was that of bilateral congenital glaucoma.

*Subsequent Clinical Course.*—The patient was admitted to the Hospital of the University of Pennsylvania, where a bilateral goniotomy was done on November 20. A small hyphema occurred in the right eye but none in the left eye. A small iridodialysis was produced at 2:30 o'clock in the right eye and at 7 o'clock in the left eye. One week later the tension was 12 mm. of mercury in the right eye and 25 mm. of mercury in the left eye. The corneas were almost clear. On December 9 the ocular tension was found to have risen to 35 mm. of mercury in the left eye; so another goniotomy was performed on this eye (fig. 6). On Jan. 3, 1946 the tension was 19 mm. of mercury in the right eye and 25 mm. of mercury in the left eye. The photophobia had disappeared. Typical ruptures were seen in Descemet's membrane of each eye. The child has been seen at regular intervals, and the tension has remained normal. His visual acuity seems excellent (fig. 7).

*Result.*—In the right eye tension was controlled by one goniotomy, and in the left eye, by two goniotomies.

CASE 6.—S. L., a 4 month old white girl, was first examined in the department of ophtalmology of the Hospital of the University of Pennsylvania on Jan. 24, 1947, at the request of the department of pediatrics.

She had been born with a diffuse port wine nevus involving both sides of her face and neck and the upper part of the thorax. Her eyeballs had been larger than normal at birth. Delivery had been spontaneous and the preg-

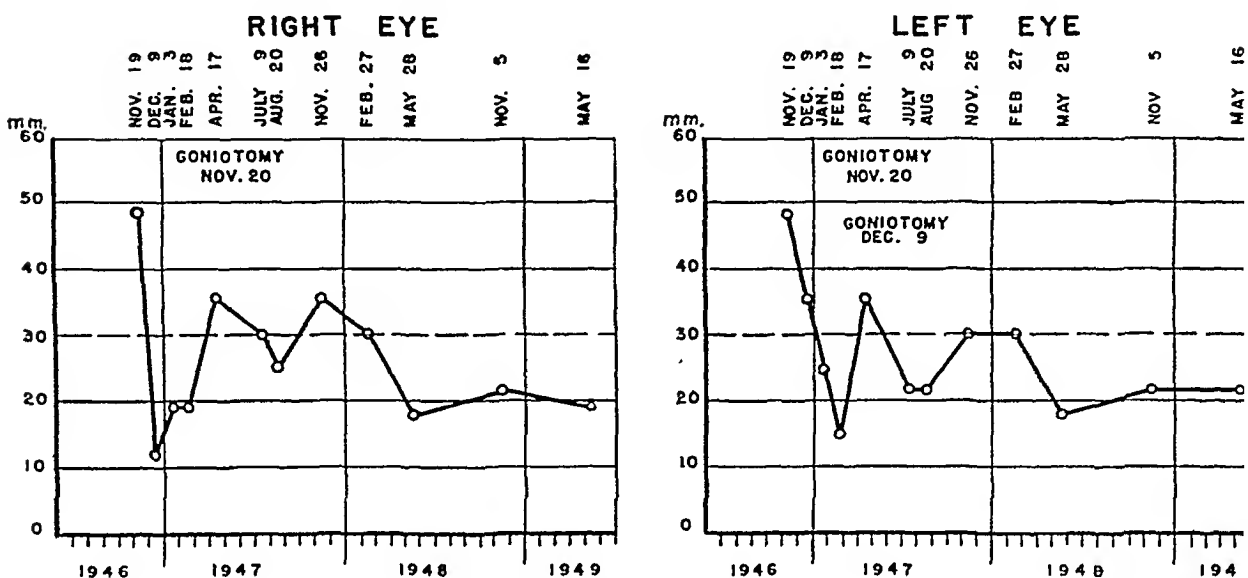


Fig. 6.—Tensions in case 5.

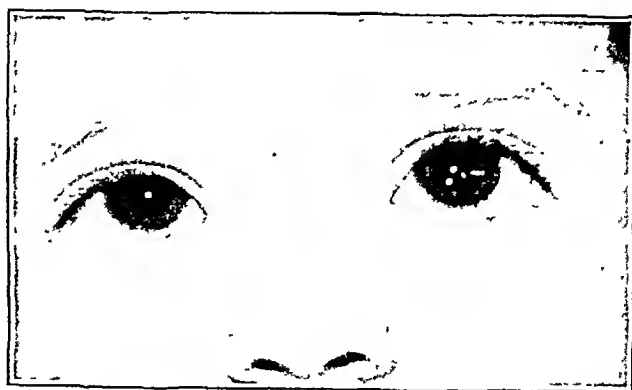


Fig. 7 (case 5).—Photograph taken at the age of 3 years, approximately two and one-half years after goniotomy.

nancy uncomplicated. The general physical examination showed nothing abnormal except for the port wine nevus. The reaction to a Kahn test was negative.

*Examination of Eyes.*—External Examination: The eyelids were normal except for a bilateral port wine nevus, part of the facial involvement. The palpebral fissures were slightly widened. The corneas were larger than normal, the right measuring 12.5 mm. and the left 13 mm. in diameter. The anterior chambers were deep. The pupils were equal and reacted promptly to light. Ocular motility seemed normal.

**Gonioscopic Examination:** A large number of anomalous blood vessels were noted in the angle of the anterior chamber of each eye, many of which extended on to the iris.

**Ophthalmoscopic Examination:** The fundi appeared normal except for suspiciously large physiologic cups. The color of the disks was normal.

**Ocular Tension:** Tension was 21 mm. of mercury in the right eye and 19 mm. in the left eye (7.5 Gm. weight).

**Impression:** A diagnosis of bilateral Sturge-Weber syndrome was considered, but the ocular tension did not confirm it.

**Subsequent Clinical Course.**—The parents were asked to bring the child in for another examination, which was done on March 29, 1947. At that time the corneas were hazy. The tension was 48 mm. of mercury in the right eye and 54 mm. in the left eye.

On March 31, bilateral goniotomy was performed. A rather severe hyphema occurred in each eye, the blood being absorbed during the week after operation. On April 7 the ocular tension was normal, but by April 27, although the corneas were clear, the ocular tension was again elevated. With the gonioscope anterior peripheral synchias were seen at the site of the goniotomy. Because of the presence of anomalous vessels in the angle, it was felt that the probable reason for the child's elevation in tension was anomalous vascularity of the uveal tract, related to the capillary hemangiomas of the face. Further goniotomy was therefore not carried out, but the child was referred to the department of roentgenology for irradiation of the eyes with a Philips tube. This was done and the child has been followed by us, in collaboration with the departments of roentgenology and pediatrics, since that time.

Within a short time after the beginning of roentgen therapy, the ocular tension fell to normal and has remained so since. The child is mentally retarded. In September 1948 she began to have convulsions, for which she was studied by the pediatrics department. It was thought that the seizures were due to an intracranial hemangioma, but roentgenograms of the skull, including an arteriogram, showed normal condition.

**Result.**—Goniotomy failed to control tension in either eye.

**CASE 7.**—R. D., an 8½ month old boy, was first seen on May 26, 1947, through the courtesy of Dr. Samuel Phillips, Allentown, Pa. His parents had taken him to Dr. Phillips because they had noticed that the right eye was larger than the left and that he had seemed sensitive to light. Dr. Phillips made a diagnosis of buphthalmos. The child's history was otherwise not remarkable. The child was an identical twin, born spontaneously at full term. His twin brother was thought to have normal eyes. The results of general physical examination were noncontributory. The reaction to a Kahn test was negative.

**Examination of Eyes.**—**External Examination:** The eyelids were normal. The right cornea was larger than the left, the respective measurements being 11 and 10 mm. Both corneas were somewhat cloudy. The right anterior chamber was slightly deeper than the left. His pupils reacted normally. Ocular motility seemed normal. The conjunctiva and sclera were healthy.

**Examination with the Slit Lamp:** The right cornea was hazy. Epithelial bedewing was present. Tears were noted in Descemet's membrane.

**Ophthalmoscopic Examination:** No definite abnormality was found. The anatomic landmarks were difficult to evaluate.

Ocular Tension: Tension was 65 mm. of mercury in the right eye and 40 mm. in the left eye (7.5 Gm. weight).

Impression: The impression was that of bilateral congenital glaucoma.

*Subsequent Clinical Course.*—A bilateral goniotomy was done on May 26, 1947, and the operation was followed by a rather marked hyphema in each eye. The hemorrhages became absorbed in the next few days. The patient had been followed at intervals of three months or less since that time, and his ocular tension has been found to fluctuate between 17 and 30 mm. of mercury in each eye (fig. 8). His corneas have remained clear, and he uses his eyes normally (fig. 9).

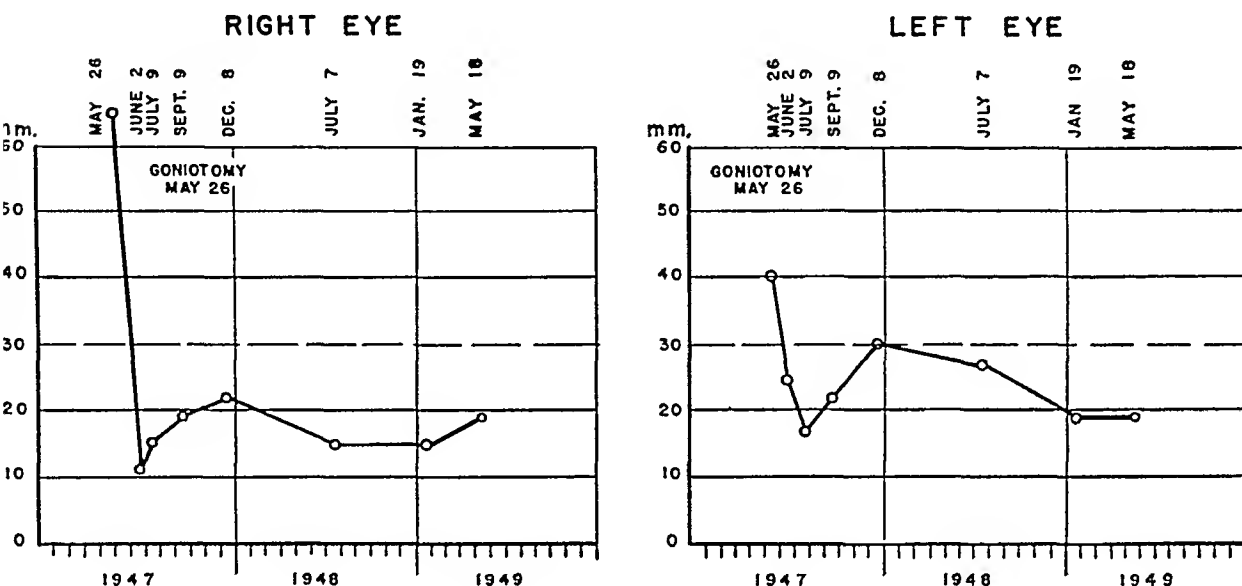


Fig. 8.—Tensions in case 7.

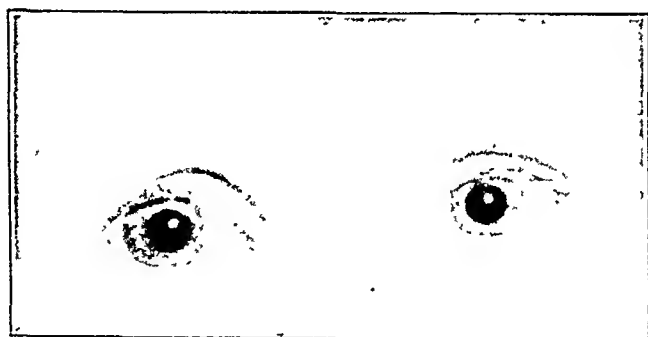


Fig. 9 (case 7).—Photographs taken at the age of  $2\frac{1}{2}$  years, two years after goniotomy.

*Result.*—Tension was controlled by bilateral goniotomy.

**CASE 8.**—R. D., an  $8\frac{1}{2}$  month old boy, was first examined on June 2, 1947, through the courtesy of Dr. Samuel Phillips, Allentown, Pa. The patient was referred for routine examination because his twin brother (case 7) had congenital glaucoma. The patient had no symptoms of ocular disease. Like his brother, he was born spontaneously at term. His development had been entirely normal.

The results of general physical examination were not remarkable. The reaction to a Kahn test was negative.

*Examination of Eyes.*—Visual Acuity: The patient used his eyes normally.

*External Examination:* No ocular abnormality was found.

*Examination with Slit Lamp:* The cornea, iris and lens of both eyes were normal. The aqueous was clear.

*Ophthalmoscopic Examination:* No definite abnormality could be found.

*Ocular Tension:* Tension was 40 mm. of mercury in the right eye and 40 mm. in the left eye

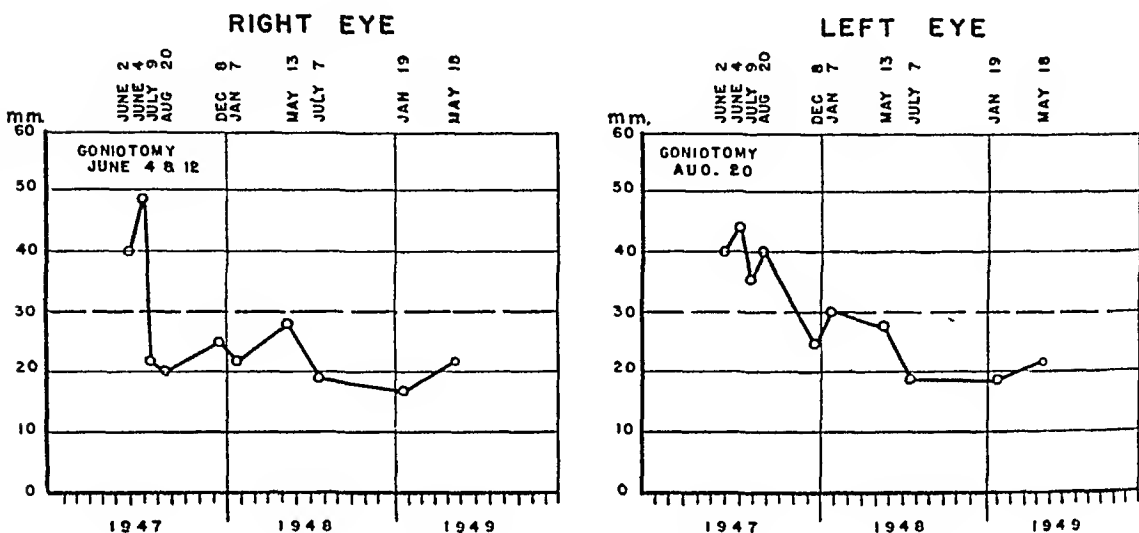


Fig. 10.—Tensions in case 8.



Fig. 11 (case 8).—Photograph taken at the age of 2½ years, nearly two years after goniotomy.

*Impression:* The impression was that of probable bilateral congenital glaucoma.

*Subsequent Clinical Course.*—The following day the tension was found to be 44 mm. of mercury in the right eye and 48 mm. in the left eye (7.5 Gm. weight). A goniotomy was therefore carried out on the right eye, which had the more elevated tension. Difficulty was encountered because of hemorrhage into the anterior chamber just as the incision was started. Operation was therefore deferred for eight days, until the eye had become quiet. The goniotomy was then completed in the right eye without difficulty. Because the patient ran a fever after operation, he was discharged from the hospital without having the

operation on the left eye. He was readmitted to the hospital in August. Tension was found to be normal in the right eye and 40 mm of mercury in the left eye (fig. 10). A goniotomy was therefore done on the left eye, without difficulty, on August 12. Convalescence was uneventful. He was discharged from the hospital in two days.

The patient also has been followed at regular intervals of no longer than three months. Tension has remained between 17 and 30 mm. of mercury, and his eyes are apparently normal (fig. 11).

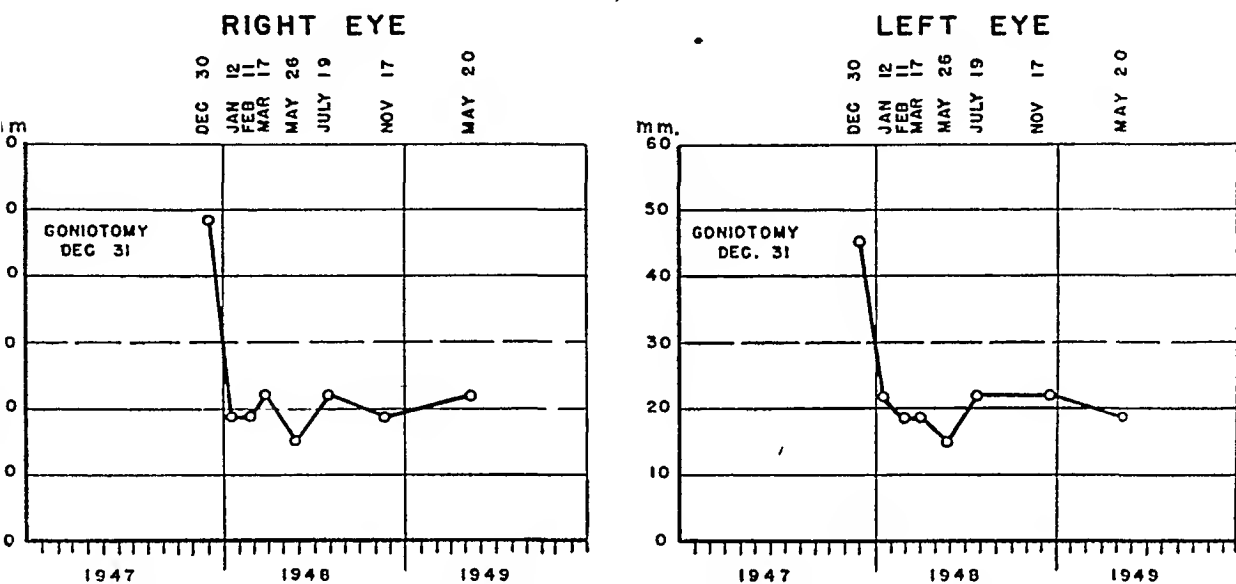


Fig. 12.—Tensions in case 9.

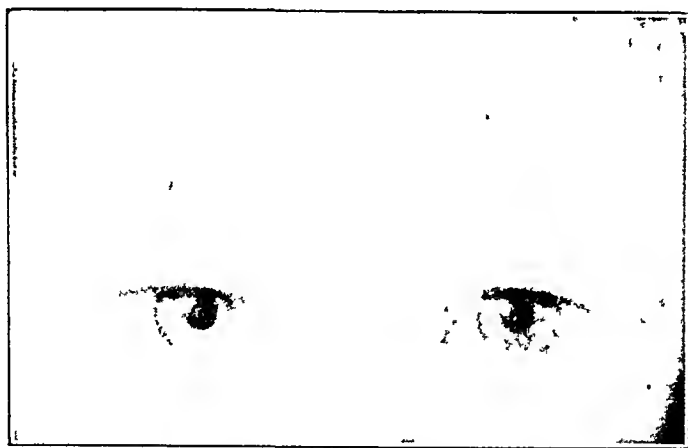


Fig. 13 (case 9).—Photograph taken at the age of 2 years, one and one-half years after goniotomy.

*Result.*—Tension was controlled by bilateral goniotomy.

**CASE 9.**—W. B., a 5 month old boy, was seen on Dec. 30, 1947, through the courtesy of Dr. Samuel Phillips, Allentown, Pa. His eyes had been noticeably large since birth. The child had been extremely photophobic the month before admission and his corneas had become gray. The child was a fraternal twin. His sister's eyes were normal. There was no family history of ocular disease except for strabismus. The child was born at full term after a normal pregnancy.

Delivery was accomplished by low forceps. His development had been normal. The results of general physical examination were not significant. The reaction to the Kahn test was negative.

*Examination of Eyes.*—Visual Acuity: His eyes would follow a dim light.

External Examination: The palpebral fissures were slightly widened. Ocular rotations were full. Each cornea was large, measuring 13 mm. in diameter. The corneas were rather diffusely hazy. The anterior chambers were deep. The pupils reacted to light. The conjunctivas and scleras were healthy.

Examination with Slit Lamp: Bedewing of the corneal epithelium was present in each eye. There was some haziness in the stroma.

Ophthalmoscopic and Gonioscopic Examinations: These studies could not be made because of the corneal haze.

Ocular Tension: Tension was 45 mm. of mercury in the right eye and 48 mm. in the left eye.

Impression: The impression was that of bilateral congenital glaucoma.

*Subsequent Clinical Course.*—On Dec. 31, 1947, bilateral goniotomy was performed, with the patient under ether anesthesia. Convalescence was uneventful. The child was discharged from the hospital on January 3. Since this time he has been followed at intervals of six weeks to three months. His ocular tension has never been above 22 mm. of mercury in either eye (fig. 12).

Subsequent ophthalmoscopic examination revealed that each disk was somewhat pale temporally and suspiciously cupped. Both corneas were clear (fig. 13).

*Result.*—Tension was controlled by bilateral goniotomy.

#### COMMENT

The results obtained with goniotomy in the treatment of 16 eyes with congenital glaucoma (table) support the claims made for the procedure by Barkan. The tension was normalized in 11 eyes, and presumably good visual acuity was retained. The disease was so advanced in the 3 eyes in which goniotomy was unsuccessful that failure was not surprising. Two of the eyes were practically blind at the time of operation, and the third eye not only was greatly enlarged but had had an unsuccessful Elliot trephination prior to goniotomy. Goniotomy also failed to control the tension in either eye of a child who had bilateral congenital glaucoma associated with bilateral port wine nevus of the face and eyelids. This condition may represent a type of glaucoma which should not be treated by goniotomy, for it is generally agreed that the cause of this entity is a nevus-like involvement of the uveal tract. Preoperative gonioscopic examination of these 2 eyes demonstrated anomalous vessels over the ciliary body which extended into the iris; the presence of these vessels probably explained the rather severe hemorrhage caused by the goniotomy.

Goniotomy was done as a primary operative procedure in 8 of the 11 eyes in which it was successful. All the children were under 1 year of age at the time of operation. Ruptures of Descemet's membrane were absent in most of these eyes, although some degree of corneal

enlargement had occurred and corneal clouding was present in the eyes of all but 1 of the patients. The exception was a boy whose identical twin had bilateral congenital glaucoma with enlargement of one cornea. As a precautionary measure, his twin was examined. On two occasions the ocular tension was 40 mm. of mercury or above; a goniotomy, therefore, was carried out on each eye, although the corneas had not been clouded.

*Results of Goniotomy in 16 Eyes with Congenital Glaucoma\**

Case No.	Eye	Age; Date of Operation	Pre-operative Tension, Mm. Hg.	Corneal Diameter, Mm.	Previous Operations	Result
1.....	OD	21 mo. June 19, 1946	33	14.0 (nearly blind)	Seven paraenteses	—
	OS	Aug. 6, 1947	38	13.0	Three paraenteses	+
2.....	OS	12 yr. June 21, 1946	35-40	14.0 (nearly blind)	None	—
3.....	OD	13½ mo. July 19, 1946	52	14.0 (nearly blind)	Trephination	—
4.....	OD	8 mo. July 29, 1946	40	13.0	Trephination	+
	OS	Sept. 9, 1946	40	14.0	Trephination	+
5.....	OD	4 mo. Nov. 20, 1946	40	13.0	None	+
	OS	Nov. 20, 1946 Dec. 9, 1946	35	13.0	None	+
6.....	OD	6 mo. Mar. 31, 1947	48	12.5 (Sturge-Weber Syndrome)	None	—
	OS	Mar. 31, 1947	54	13.0 (Sturge-Weber Syndrome)	None	—
7.....	OD	8½ mo. May 26, 1947	65	11.0	None	+
	OS	May 26, 1947	40	10.0	None	+
8.....	OD	8½ mo. June 4, 1947	44	10.0	None	+
	OS	June 12, 1947 Aug. 12, 1947	48	10.0	None	+
9.....	OD	5 mo. Dec. 31, 1947	45	13.0	None	+
	OS	Dec. 31, 1947	48	13.0	None	+

\* The results of goniotomy were successful (+) in 11 eyes and the operation failed (—) in 5 eyes, 3 of which were nearly blind and 2 had the Sturge-Weber Syndrome.

Claims for the successful treatment of congenital glaucoma, particularly when a small number of cases are involved, must necessarily take into consideration the occasional spontaneous resolution of the disease which does occur. An example was the right eye of A. O. K. (case 2), who at the age of 12 had normal tension in his right eye, vision of 6/9, a healthy optic nerve and a full visual field, in spite of definite corneal enlargement and classic ruptures of Descemet's membrane due to congenital glaucoma, which had cleared spontaneously. The fellow eye showed similar corneal enlargement with ruptures of Descemet's membrane but was nearly blind and had greatly increased tension with atrophy of the optic nerve.



Goniotomy possesses many advantages over other operations for congenital glaucoma. It seems very effective if done early. A second operation was done only once in our series. There seems to be little danger from the procedure. As pointed out by Barkan, the chief danger is hemorrhage into the anterior chamber. The blood is usually absorbed promptly. There is danger of injury to the ciliary body and of producing iridodialysis. No cases of sympathetic ophthalmia have been reported. Subluxation of the lens must be considered a possibility, particularly in enlarged eyes in which the zonular fibers are taut. In several of our patients peripheral anterior synechias developed after operation, but these adhesions can be avoided by the postoperative injection of air into the anterior chamber. We attempted to use the goniotomy lens twice in this series of cases but found that it offered no advantages and served only to make the operation more difficult.

The operation seems to be permanently successful. Patients reported on in this paper have all been followed one and one-half years or longer, and in none of the eyes in which the goniotomy was successful has the tension again become elevated. At the time of his last report, Barkan had followed some of his patients as long as ten years. No late complications have been observed by us. The operation, therefore, tends to circumvent the objections to the various filtration procedures, such as late infection and cataractous changes.

#### SUMMARY

1. The tension in 11 of 14 eyes with congenital glaucoma was successfully lowered by goniotomy.
2. Failure occurred only in the eyes in which the disease was advanced.
3. Goniotomy failed to control the tension in the two eyes of the same patient in which the elevated tension was associated with bilateral port wine nevus of the face and eyelids.
4. Goniotomy seems to be a fairly simple and safe procedure.
5. All the patients successfully treated by goniotomy have been followed two years or longer.

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## OPERATIONS FOR BLEPHAROPTOSIS

M. I. STECKLER, M.D.  
LOS ANGELES

**A** DROOPING lid that covers a normal eye renders a good eye useless, disfigures a face and shuts in a personality.

The problem of ptosis looms before the ophthalmologist at various times and must be faced. The surgical procedure used depends on the type of training (ophthalmologist or plastic surgeon) and where the training was obtained. The ophthalmologist uses one of the many procedures for correction of the ocular muscles, whereas the plastic surgeon usually prefers one utilizing the occipitofrontalis muscle. Constantly good end results, like those in every other routine, depend on frequent practice and experience. Improvements in technics have continued to be made; in my opinion, one procedure (the Dickey method) offers constantly good end results even for the occasional operator if the various steps are faithfully followed. When the ptosis is of recent origin, less than one year, one is chiefly concerned with finding the cause. When the ptosis is of several years' duration, one is chiefly concerned with surgical correction, though the cause is not entirely forgotten.

There are two general types of ptosis, either of which may be partial or complete, unilateral or bilateral: congenital and acquired. Both the congenital and the acquired type may be further subdivided into (*a*) true ptosis and (*b*) pseudoptosis.

### CAUSES OF PTOSIS

The causes of congenital ptosis are: (*a*) weakness of the levator palpebrae superioris (striate) muscle, or Müller's (smooth) muscle of the lid, due to progressive muscular dystrophy; (*b*) disorder of a peripheral nerve to the levator, or (*c*) disorder of the central nervous system.

Causes of acquired ptosis are usually intoxications, either acute or subacute: (*a*) syphilis or leprosy involving the roots, the nucleus, the supranuclear centers or the cortical centers of the third nerve; (*b*) lesions of the brain substance, such as hemorrhage, abscess formation or tumor; (*c*) various diseases of the nervous system, such as myas-

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thenia gravis and multiple sclerosis, and (d) trauma, accidental or surgical. In cases of the acquired type due to intoxications, surgical intervention should not be contemplated sooner than one year.

Causes of pseudoptosis are (a) abnormal widening of the opposite palpebral fissure<sup>1</sup>; (b) disease or increased weight of the lid, such as a trachomatous infiltration, tumors of the lid, spasm of the orbicularis muscle and neurofibromatosis; (c) paralysis of the superior rectus muscle of one eye with spasm of the inferior oblique muscle of the affected eye, causing the cornea to turn up under the lid, with production of an apparently severe ptosis of one eye when no ptosis is present<sup>2</sup>; (d) ptosis which is bilateral but of the outer half of the eye only.

#### CLINICAL CLASSIFICATION OF TRUE PTOSIS<sup>2</sup>

True ptosis may be classified clinically as follows:

Type 1: Unilateral ptosis without involvement of the homolateral superior rectus muscle.

Type 2: Unilateral ptosis with involvement of the homolateral superior rectus muscle.

Type 3: Bilateral ptosis without involvement of the superior rectus muscles.

Type 4: Bilateral ptosis with involvement of the superior rectus muscles.

Type 5: Unilateral ptosis with weakness of both superior rectus muscles, more pronounced in the homolateral eye.

Type 6: Ptosis with more or less severe paralysis of the third nerve and even of the sixth nerve.

Type 7: Ptosis with the classic jaw-winking reflex, the Marcus Gunn syndrome of misdirection of the developing fifth cranial nerve and oculomotor nerve fibers.

Type 8: Ptosis with the Duane retraction syndrome.

Type 9: Ptosis with neurofibromatosis.

#### CORRECTION OF PTOSIS

For cosmetic reasons, and because of the mental strain produced by the facial disfiguration of ptosis, the condition should be corrected, by surgical means or otherwise. Secondary deformities or effects of ptosis of great import are (a) amblyopia, due to obstructed vision;

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1. Meyer, S. J.: *Diagnosis and Treatment of Blepharoptosis*, Illinois M. J. **91**:89-92 (Feb.) 1947.

2. Spaeth, E. B.: *Ptosis, Congenital, Classification: Principles of Surgical Correction*, Tr. Am. Acad. Ophth. (1942) **47**:285-301 (March-April) 1943.

(*b*) change in curvature of the spine<sup>3</sup>; (*c*) torticollis; (*d*) spasm of occipitofrontalis muscle, and, last, but not least (*e*) a feeling of inferiority.

The nonsurgical method of correction of ptosis is use of a crutch glass (attached to the spectacles) for the drooping lid. This is for the patient who refuses operation or for some medical reason (anesthesia of the cornea; complete palsy of the nerve) cannot undergo surgical treatment.

The operations for ptosis comprise less than 1 per cent of all surgical procedures on the eye and its appendages.<sup>1</sup> To raise the lid so that it resembles a normal lid, so opening the patient's personality to the outside world and revealing the glint in his eye, is an incomparable satisfaction to the surgeon for work well done and skill attained.

Before an attempt at surgical correction is made, data should be obtained on the following:

(1) Vision in the two eyes and the presence of amblyopia, diplopia or fusion; (2) the sensibility of the cornea, as an estimate of its ability to withstand exposure; (3) the vertical width of the palpebral fissure with the eyes looking straight ahead, with the eyes looking up and with the eyes looking down; (4) estimation of the strength of the elevator power of the muscles of the eyelid when acting alone by computing the measurements in (3) with the patient employing the aid of the frontalis muscle, which arches the brow and corrugates the forehead, with the measurements when the brow is depressed by the fingers of the observer; (5) exophthalmometric reading, if proptosis is suspected; (6) extraocular motility of each eye, especially that of the superior rectus muscle, and the fields of fixation, and (7) effect of cocaine on the smooth muscle of the lid.

The four basic surgical methods for correction of ptosis are (1) shortening of the lid (Kuhnt-Heisrath operation), (2) shortening of the levator palpebrae superioris muscle (Blaskovics, 1923), (3) utilization of the superior rectus muscle (Motias, 1898), (4) utilization of the occipitofrontalis muscle (Dransart, 1879). There are many modifications of these four basic operations for the correction of ptosis, their number indicating efforts to achieve a technic with constantly good results.

Surgical correction for the various types of true ptosis are suggested for the occasional operator as follows:

Type 1: Dickey operation for ptosis.

Type 2: Dickey operation (if the inferior oblique of the affected eye is normal and there is no hypotropia. If hypotropia is present,

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3. Meek, R. E.: Ptosis: Applied Anatomy of Eye; Relation to Ophthalmic Surgery, Arch. Ophth. 26:494-513 (Sept.) 1941.

this should first be corrected or the procedure indicated for type 4 carried out.)

Type 3: Dickey operation bilaterally.

Type 4: First choice: Dickey operation after advancement of both superior rectus muscles and recession of both inferior rectus muscles. Second choice: utilization of occipitofrontalis muscle.

Type 5: Dickey operation for ptosis after advancement of the superior rectus muscle on the affected side. Recession of the overacting inferior oblique for relief of diplopia and other indicated surgical correction of extraocular muscles.

Type 6: Crutch glass as first choice, or some utilization of the occipitofrontalis muscle (combined with measures to place the deviating eye in the forward position, such as recession of the external rectus muscle and advancement with resection of the internal rectus muscle, provided no corneal anesthesia is present).

Type 7: Dickey operation.

Type 8: Recession of the internal rectus muscle, followed by the Dickey operation if correction of ptosis is insufficient. The first procedure frequently corrects the retraction syndrome and thereby greatly improves the ptosis.

Type 9: Utilization of the occipitofrontalis muscle after plastic surgical procedures.

*Kuhnt-Heisrath Operation.*—This procedure consists in excision of a great part of the tarsus, in an effort to lighten the weight of the lid, as in cases of trachoma.

*Blaskovics Operation.*—There is no absolute means of measuring in millimeters the amount of muscle to be shortened in order to correct a given degree of ptosis, but one can follow the rule<sup>4</sup> that removal of about 2 mm. of muscle or of about 1 mm. of cartilage is required to correct 1 mm. of ptosis. Thus, considering a normal width of fissure as about 11 mm., if there is a deficiency in width of about 6 mm., 12 mm. of muscle must be removed to secure a width of fissure of 11 mm.

The mere fact that there are no absolute means of measuring the amount of levator muscle to be shortened, or the strength of the weakened levator, permits an uncontrolled variable to be ever present, so that, in the hands of most operators, the results of the Blaskovics operation cannot be depended on.<sup>5</sup> Undercorrection is the rule, although occasional overcorrection in the lateral half occurs.

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4. Modified Blaskovics Operation for Ptosis, *Bull. Pract. Ophth.* **12**:7-9 (Jan.) 1942.

5. Fink, W. H.: Surgical Management of Ptosis, *Journal-Lancet* **60**:245-246 (May) 1940.

*Motais Operation.*—Most surgeons insist that the action of the superior rectus be strong<sup>4</sup>; yet the procedure may also be successful when the superior rectus is partially paralyzed, provided there is no hypotropia and the inferior oblique is normal. If both the superior rectus and the inferior oblique are paralyzed, this operation is not indicated. It is usually contraindicated in cases of unilateral ptosis, as there exists the danger of producing postoperative hypotropia and diplopia. If the cornea is anesthetic, complications may arise, as in sleep the lower part of the cornea is always exposed after this operation. However, when successfully performed, the Motais operation provides for the synchronous movement of the upper lid with that of the globe in looking up and down. Good elevation of the lid is secured, and a satisfactory lid fold develops. An important criticism of this operation is the resultant notching of the upper lid, which may necessitate a graduated tarsectomy at the time of the original operation, or later. Another important reason for failure is that the sutures employed in attaching the tongue of the superior rectus muscle to the tarsus may pull out or the adhesions produced between the upper lid and the globe may pull out or become stretched. If the entire width of the superior rectus muscle is attached to the lid without severing its tendinous attachment to the globe, symblepharon with entropion and distichiasis results.

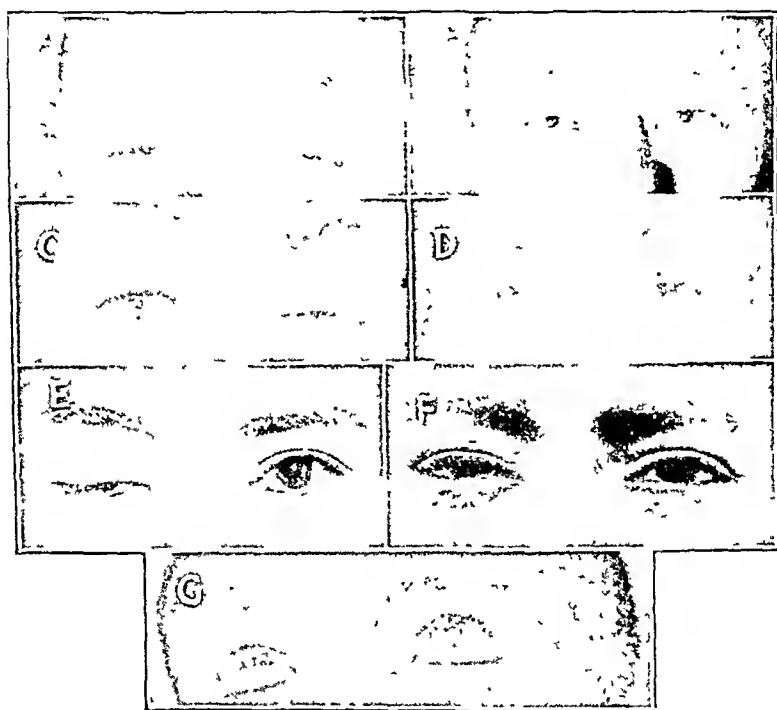
Diplopia may result if the superior rectus muscle is weakened too much. However, if only the middle third of the muscle is used, the small amount of diplopia produced will not be annoying. A disturbance in the coordination of the act of closure of the lids results, and the globe is prevented from rolling up normally.

A study of the extraocular muscles should be made in all cases, as there is often a weakness of the elevator muscles of the globe in association with ptosis. Such a hypotropia should first be remedied before any surgical correction of the ptosis is attempted, especially if one contemplates utilization of the superior rectus muscle to lift the ptosed lid. Any exotropia or esotropia should be corrected first before operation for ptosis is done.

The use of a fascia lata sling attached to each end of the tarsus and running under the superior rectus muscle has come into favor in recent years (Dickey operation); this procedure removes many of the disadvantages of the Motais operation. However, the innervation, origin and course of the muscle fibers of the levator and the superior rectus are the same, so that no reeducation is required for the new function of the muscle. The easiest approach in this operation is through the conjunctiva.

One should note the position of the upper lid fold of each eye before operation, so that the new lid fold may be placed in its proper place at the time of operation.

*Dransart Operation.*—This procedure, which consists in the production of adhesions between the frontalis muscle and the upper lid, although easy of accomplishment, is not good surgery. It leads to a straight upward pull on the lid and accentuates the already present smooth lid effect. The implantation of deep long sutures and buried strips of epidermis is open to serious objections. If all the elevators of the globe and lid are paralyzed, it may be necessary to use fascia lata or fibers of the orbicularis. While such an operation probably



A-G, results of the Dickey operation for ptosis. A, C and E are preoperative photographs; B, D and F show postoperative results.

A (case 1, age 29), severe bilateral congenital ptosis, showing extended chin, elevated eyebrows and corrugated forehead, timidity and inferiority complex.

B (case 1), correction of ptosis by the Dickey operation. Note absence of the elevated brows, corrugated forehead and extension of the chin. The lids moved up and down like normal lids.

C (case 2; age 49), severe bilateral acquired ptosis, of undetermined cause, more pronounced on the left side.

D (case 2), correction of ptosis by the Dickey operation (bilateral). The glint in the eyes is there.

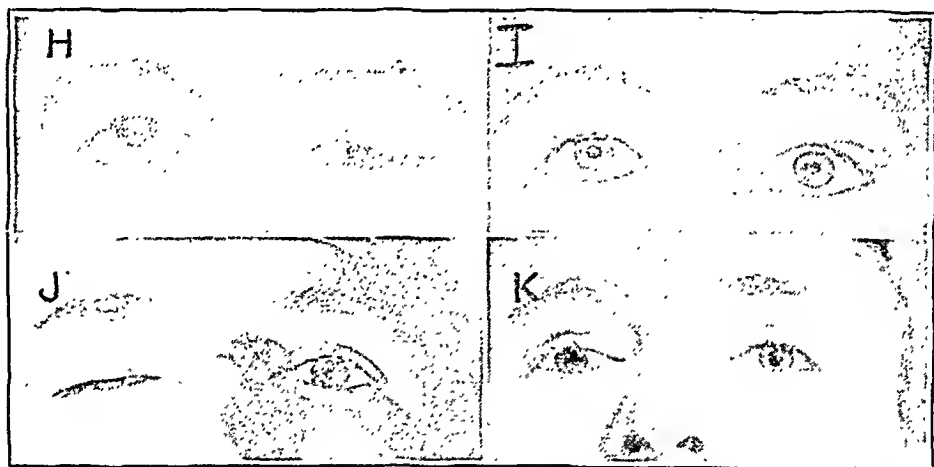
E (case 3; age 24), very severe unilateral congenital ptosis.

F (case 3), correction of unilateral ptosis by the Dickey operation.

G (case 3), postoperative photograph, showing that the natural, synchronous upward movements of the lids.

constitutes the type of surgical correction most frequently performed, the end results are usually far from satisfactory. If the lower, or lid, attachment of the implantation is in the middle third of the tarsus, a postoperative notching may develop, which is unsightly and may be corrected later only by a tarsectomy. Hence the lid attachment of the implantation should be at the junction of the middle and the inner third, as this is usually the highest part of the upper lid and attachment here gives a better cosmetic result.

If diplopia is present before operation when the ptosed lid is raised, an attempt should be made to correct it before correction of the ptosis. If the ptosed eye is amblyopic, the danger of disturbing fusion or of producing postoperative diplopia is negligible. If the tactile sensibility of the cornea is lost, one can be almost certain that uncovering the cornea will sooner or later result in neuroparalytic keratitis, with its serious consequences.



*H-K*, results of the Weiner-Alvis modification of the operation utilizing the occipitofrontalis muscle. *H* and *J* are preoperative, and *I* and *K* postoperative, photographs.

*H* (case 4; age 22), severe unilateral congenital ptosis and concomitant hypotropia.

*I* (case 4), correction of hypotropia and correction of ptosis by modified Dransart operation, using fascia lata. Results are fair, but not as good as with the Dickey operation in case 3. The corrected left lid has flat appearance and an unsightly fold.

*J* (case 5; age 25), severe ptosis and concomitant severe unilateral congenital hypotropia.

*K* (case 5), correction of ptosis and hypotropia by a modified Dransart operation, using fascia lata. Results are fair but not as excellent as in case 3. The affected lid does not move up and down like its fellow, but must be raised by elevating the brow.

*Dickey Operation for Ptosis.*—The many surgical procedures for the correction of ptosis indicates that satisfactory results cannot always be depended on, even in the best of hands. Because of the relatively rarity



of this condition, most surgeons do not have the opportunity to perform many operations to improve their technic, and the search for one procedure which can be depended on for satisfactory end results in most cases continues, as new improvements are tried. I have heard several eminent ophthalmologists in various parts of the country state that they use the Blaskovics procedure in all cases of ptosis. Plastic surgeons say they use some modification of the Dransart technic in all cases of ptosis. It is my opinion that the Dickey (modified Motaïs) operation will give constantly excellent results in any type of ptosis except as noted later in the contraindications, in which case a Dransart operation<sup>6</sup> or one of its modifications is used. The technic of the Dickey operation can be obtained elsewhere.<sup>7</sup> The Dickey operation for ptosis has the following advantages:

1. The corrected height of the lid can be depended on to remain where it is fixed at the operating table. No overcorrection or undercorrection, which may not adjust itself after operation, is necessary.
2. The operation is not difficult to perform (the conjunctival route is easier than the external, or skin, route).
3. Neither the superior rectus muscle nor any portion of it is detached from the globe.
4. The whole muscle, rather than the fibers of its middle third only, lends itself to the support of the lid.
5. There is a minimum chance of any sutures pulling loose.
6. It produces a firm attachment between the superior rectus muscle and the upper lid.
7. The cosmetic and functional results are very good in suitable cases.
8. A wide palpebral fissure, or one resembling the unaffected side, may be secured, as desired.
9. The fissure resembles the normal elliptic ones, and the lid fold is usually satisfactory.
10. The lid follows the eye in its vertical movements.
11. There is no contraindication, no diplopia of any importance in cases of unilateral ptosis provided the superior rectus of the affected side is normal.
12. If, for any reason, the operation must be undone, this can be achieved in the office simply by everting the lid and cutting one arm of the fascia.

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6. Rosenberg, S.: Ptosis: Fascia Lata Transplant, *Am. J. Surg.* **47**:142-148 (Jan.) 1940.

7. Cordes, F. C., and Fritsch, U.: Dickey Operation for Ptosis: Results in Twenty-One Patients and Thirty Lids, *Arch. Ophth.* **31**:461-468 (June) 1944.

The dressing is an important part of the technic. The Friedenwald procedure, in which a lower lid suture is inserted to pull the lower lid upward over the cornea (to avoid exposure keratitis) and lend temporary support to the upper, or corrected, lid is excellent.<sup>8</sup>

Contraindications to the Dickey operation for ptosis are (1) anesthesia of the cornea, (2) paralysis of the superior rectus and inferior oblique of the affected eye, (3) neurofibromatosis and (4) complete paralysis of the third nerve.

Without a doubt, any operative procedure which corrects a condition so that a resemblance to the normal structure and function is established is the one of choice. In accordance with this precept, the Blaskovics operation would be foremost if the operator could depend with certainty on his results. Otherwise, the results of the Dickey operation, though not restoring the normal structure, can be depended on even by the occasional operator and gives definitely better cosmetic and function results than utilization of an occipitofrontalis muscle or other procedures.

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8. In a child aged 14 months, for whom pictures were not available, severe unilateral congenital ptosis, producing head tilt to the right shoulder and extension of the chin toward the left shoulder, was corrected by the Dickey operation, with alleviation of the ptosis, the head tilt and the rotation of the chin. The corrected lid now moves up and down synchronously with its unaffected fellow.

# Ophthalmologic Reviews

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## NEUROMYELITIS OPTICA (DEVIC'S DISEASE)

Presentation of Five Cases, with Pathologic Study, and Review of Literature

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NEW YORK

**S**UDDEN, complete binocular loss of vision in a healthy young adult is undoubtedly a major catastrophe to the patient. When examination of the afflicted person reveals no pathologic basis for the blindness, it becomes a problem of major importance to the ophthalmologist. Such is often the case in the rare syndrome called neuromyelitis optica, or Devic's disease.<sup>1</sup> This condition is commonly ushered in by sudden, total blindness, followed by a severe, rapidly ascending inflammation of the spinal cord, terminating in death. The cause of this malady is unknown, and there is no known method of effective therapy. Pathologically, acute necrosis of nerve tissue is observed, principally in the optic nerves and the spinal cord. Histologically, destruction of myelin sheaths, axis-cylinders, nerve cells and neuroglia is seen, accompanied with infiltration of white blood cells and with a feeble attempt at repair by the nerve tissue.

Neuromyelitis optica is but one of the group of so-called demyelinating diseases of the central nervous system which exhibit this pathologic picture. The other components of this group are: (1) multiple sclerosis, the commonest; (2) the acute disseminated encephalomyelitis that follow vaccination, foreign serum therapy and the acute infectious diseases of children, and (3) the diffuse scleroses, including Schilder's disease (progressive subcortical encephalopathy), Pelizaeus-Merzbacher disease (aplasia axialis extracorticalis congenita), Krabbe's disease (infantile familial diffuse cerebral sclerosis, Scholz's disease (juvenile familial diffuse cerebral sclerosis) and Baló's disease (an infantile demyelinating encephalopathy). These are all acute processes with a high mortality rate, with the exception of multiple sclerosis. They are all commonest in the first half of the average life, multiple sclerosis and neuromyelitis optica occurring usually in young adults and the others oftenest in children. The clinical picture varies with

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1. This syndrome is also known as myelitis with optic neuritis (Dreschfeld), optic neuritis and myelitis (Sharkey), neuroptic myelitis (Devic), ophthalmoneuromyelitis (de Lapersonne), ophthalmo-encephalo-myelopathy (Barrera) and optic encephalomyelitis (Klar). In addition to the Latin term, neuromyelitis optica, the condition is frequently called optic neuromyelitis or, more simply, neuromyelitis.

the location of the lesions in the nervous system but always shows a decided trend toward involvement of the optic pathway. Microscopically, the lesions of all these syndromes are similar. The differential diagnosis of the various types is a matter of standing dispute, largely because there is no generally accepted terminology. In the absence of knowledge of their etiology, these diseases have been designated by names suggestive of the anatomic distribution or histologic characteristics of their lesions. Pathologic classification fails, because they merge into one another in such a way as apparently to constitute different stages of a single disease process. Clinical classification is unsuccessful, for the same reason; it does not include the transitional types that exhibit features common to two or more pathologic varieties. The only available classification today attempts to correlate both the clinical and the pathologic characteristics and to include the transitional forms. Future investigation may disclose that these clinicopathologic distinctions do not actually correspond to differences in etiology, but that they are the result of differences in severity of the process, the heredity of the patient, the age of the patient, the nature of the precipitating events and the constitution and immunity of the patient. As a group, the demyelinating diseases embody one of the outstanding unsolved problems in the field of medicine.

The preceding paragraphs may suggest the reasons for the ensuing detailed discussion of a rarity like neuromyelitis optica: 1. Although generally considered a rare and unimportant disease, it assumes a new importance if it is a form of multiple sclerosis, as is often proposed today. With its high mortality rate, neuromyelitis optica furnishes more material for pathologic study than multiple sclerosis. 2. More important, because neuromyelitis optica is often fatal in the early acute stage, its study may fill an important void in the pathology of multiple sclerosis. 3. Even though the two diseases are not identical, the study of neuromyelitis optica is worth while because of their close similarity. 4. The fact that the optic apparatus is always involved warrants the attention of the ophthalmologist. 5. Finally, because the subject of the place of neuromyelitis optica among the demyelinating diseases has not been reviewed in the English ophthalmologic literature since 1927, it is time for a reevaluation in the light of recent neuropathologic developments.

#### HISTORICAL REVIEW

*Earlier Literature.*—Convinced of the value of ophthalmoscopic study in the diagnosis of lesions of the brain, Allbutt<sup>2</sup> a physician at the Leeds Infirmary in the last century, decided to investigate the

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2. Allbutt, T. C.: On the Ophthalmoscopic Signs of Spinal Disease, *Lancet* 1:76-78, 1870.

fundus in cases of disease of the spinal cord. Cognizant of the fundus changes in tabes dorsalis, he looked instead for patients with acute processes, either traumatic or inflammatory. In 1870 he published his results in the *Lancet*: (1) In 17 cases of acute trauma to the spinal cord no pathologic change in the fundus had been noted, and (2) of 5 cases of acute nontraumatic myelitis, optic neuritis had appeared twelve weeks after the spinal symptoms in 1. Subsequent authors have considered the last case the first instance of neuromyelitis optica reported in the literature. With no autopsy, Allbutt was unable to elucidate the strange combination of lesions in the optic nerve and spinal cord, but he hypothesized an extension of meningitis from the cord to the base of the brain, and thence to the optic nerves.

The honor of the first thorough clinical description of neuromyelitis optica must be awarded to Erb,<sup>3</sup> who in 1879 reported a case of "myelitis transversa dorsalis with neuritis descendens opticorum." The course in his case was prolonged, but the patient eventually recovered both vision and mobility of the extremities. One year later Seguin<sup>4</sup> presented 2 cases of "optic neuritis and subacute transverse myelitis" before the New York Neurological Society; his patients also survived, after a protracted siege. Both Erb and Seguin expressed the opinion that the coincidence of disease of the optic nerves and that of the spinal cord was an accident, with no causal or pathologic relation. In 1882 Chisholm<sup>5</sup> published the first case report of this syndrome in the American ophthalmologic literature. Achard and Guinon<sup>6</sup> in 1889 published the first pathologic study of neuromyelitis optica, describing the complete disappearance of myelin sheaths in the optic nerves of their patient.

In 1894 Devic<sup>7</sup> summarized the reported cases before the French Congress of Medicine at Lyon and coined the terms *neuro-myélite* and *neurooptico-myélite* for this optic neuritis (he included both papillitis and retrobulbar neuritis) accompanied with acute myelitis and occa-

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3. Erb, W.: Ueber das Zusammenvorkommen von Neuritis optica und Myelitis subacuta, Arch. f. Psychiat. **10**:146-157, 1880.

4. Seguin, E. C.: On the Coincidence of Optic Neuritis and Subacute Transverse Myelitis, J. Nerv. & Ment. Dis. **7**:177-188, 1880.

5. Chisholm, J. J.: An Obscure Case in Nerve Pathology Accompanying Optic Neuritis, Arch. Ophth. **11**:239-242, 1882.

6. Achard, C., and Guinon, L.: Sur un cas de myélite aiguë diffuse, avec double névrite optique, Arch. de méd. expér. et d'anat. path. **1**:696-710, 1889.

7. Devic, M. E.: Myélite aiguë dorso-lombaire avec névrite optique: Autopsie, Congrès français de Médecine, Première Session, Lyon, 1894, **1**:434-439, 1895: abstracted, Myélite subaiguë compliquée de névrite optique, Bull. méd., Paris **8**: 1033, 1894.

sionally with other neurologic symptoms. He found 16 cases<sup>8</sup> in the literature, with 4 deaths, and added a fatal case of his own, with autopsy. Discarding the various theories previously advanced to explain the pathogenesis of this syndrome, Devic admitted that nothing was known of either the etiology or the pathogenesis of these anatomically separated lesions, and he stressed the importance of a complete ophthalmologic examination as an approach to the solution. Devic's case report and pathologic observations were expanded into a doctoral thesis by one of his pupils, Gault.<sup>9</sup> Since that time the syndrome has frequently been called Devic's disease.

Survey of the literature on neuromyelitis optica by Goulden<sup>10</sup> in 1914 disclosed 51 case reports,<sup>11</sup> his own making the fifty-second

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8. Devic reviewed the following reports: (a) Abadie, M.: De l'atrophie des nerfs optiques dans le mal de Pott, *Bull. Soc. de chir.* **1**:26-32, 1876. (b) Steffan, P.: Beitrag zur Lehre des Zusammenhanges der Erkrankungen der Sehnerven mit denen des Rückenmarkes, *Ber. d. Ophth. Gesellsch.* **17**:90-105, 1879. (c) Erb.<sup>3</sup> (d) Seguin.<sup>4</sup> (e) Chauvel, J.: Névrite optique double avec myélite aiguë temporaire, *Bull. et mém. Soc. de chir. de Paris* **6**:512-517, 1880. (f) Noyes, H. D.: Acute Myelitis mit doppelseitiger Neuritis optica, *Arch. f. Augenh.* **10**:331-337, 1881. (g) Rumpf, T.: Zur Wirkung des faradischen Pinsels bei einem Fall von Neuritis optica und Myelitis transversa, *Deutsche med. Wchnschr.* **7**:442-443, 1881. (h) Dreschfeld, J.: On Two Cases of Acute Myelitis Associated with Optic Neuritis, *Lancet* **1**:8-9 and 52-53, 1882. (i) Sharkey, S. J.: Embolism of the Right Middle Cerebral Artery Producing Left Hemiplegia and Hemianesthesia: Absorption of a Large Portion of the Right Hemisphere; Death Seven Years Later, *M. Times & Gaz.* **1**:846-847, 1884. (j) Knapp, H.: Ein Fall von acuter Myelitis mit beiderseitiger Ophthalmoplegia und Stauungspapille berichtete, *Klin. Wchnschr.* **22**:835-836, 1885. (k) Firth, R.: Double Optic Neuritis with Paralysis of One Arm, Following an Injury to the Spine, *Practitioner* **36**:426-429, 1886. (l) Achard and Guinon.<sup>6</sup> (m) Drake-Brockman, E. F.: A Case of Double Optic Neuritis Dependent on Spinal Disease, *Brit. M. J.* **2**:77-78, 1892. (n) Fuchs, S.: Klinische und anatomische Untersuchungen über einen Fall von multipler Neuritis mit Erkrankung der NN. optici, *Deutsche Ztschr. f. Nervenkrank.* **4**:38-78, 1893. (o) Schanz, F.: Ueber das Zusammenvorkommen von Neuritis optica und Myelitis acuta, *Deutsche med. Wchnschr.* **19**:615-617, 1893.

9. Gault, F.: De la neuromyéélite optique aiguë, Thesis for the Doctorate, Lyons, no. 0981, 1894, p. 104.

10. Goulden, C.: Optic Neuritis and Myelitis, *Tr. Ophth. Soc. U. Kingdom* **34**:229-252, 1914.

11. In addition to the papers previously discussed by Devic, Goulden reviewed the following publications: (a) Dedone, P.: Étude sur la névrite optique, Thesis, Paris, no. 202, 1875, p. 50. (b) Thorowgood, J. C.: Case of Optic Neuritis, with Complete Loss of Vision: Recovery under Treatment, *Tr. Clin. Soc. London* **8**:80-83, 1875. (c) Putzel, L.: Remarks on a Case of Neuritis with Secondary Inflammation in the Spinal Cord, *M. Rec.* **15**:390-392, 1879. (d) Rieger, F., and Forster, R.: Auge und Rückenmark, *Arch. f. Ophth.* **27**:109-202, 1881. (e) Schluter, F.: Ueber Neuritis optica, *Inaug. Dissert.*, Berlin, G. Schode, 1882, p. 42. (f) Sharkey, S. J., and Lawford, J. B.: On a Case of Acute Optic Neuritis

reported case. Goulden claimed that his patient, a white man aged 60, was older than any of the preceding patients; the patient suffered nearly complete loss of vision in six days, followed by severe ascending myelitis and death sixteen days after onset of the visual difficulty. According to Goulden's survey, blindness preceded the spinal syndrome in over 80 per cent of the cases. Ophthalmoscopically, optic neuritis (ranging from slight hyperemia of the disk to full-blown edema with dilated, tortuous veins, hemorrhages and exudates) was seen; retrobulbar neuritis was rare. He found nothing characteristic about the myelitis; the symptomatology was that of ordinary acute ascending inflammation of the cord. Goulden stressed the similarity of the course of the myelitis and the optic neuritis; both showed slight symptoms in the beginning, both progressed to a period of great intensity and, if death did not supervene, both retrogressed to complete, or almost complete, recovery. From his study of the pathology, Goulden decided that the two processes, visual and spinal, were due to a common infectious cause.

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Associated with Acute Myelitis, *Tr. Ophth. Soc. U. Kingdom* 4:232-243, 1884. (g) Knapp, H.: Ueber einen Fall von acuter Myelitis mit beiderseitiger Ophthalmoplegia und Stauungspapille, *Neurol. Centralbl.* 4:502-503, 1885. (h) Picqué, L.: Étude critique sur l'anatomie pathologique et al pathogénie des névrites optiques, *Arch. d'opht.* 18:420-435, 1888. (i) Eskridge, J. T.: Acute Myelitis Preceded by Acute Optic Neuritis, *J. Nerv. & Ment. Dis.* 17:609-615, 1890. (j) Elschnig, A.: Klinischer und anatomischer Beitrag zur Kenntniss der acuten retrobulbären Neuritis, *Arch. f. Augenh.* 26:56-80, 1893. (k) Mahokian, P. A.: Neuritis optica bei Myelitis acuta, *Inaug. Dissert.*, Berlin, O. Francke, 1893, p. 30. (l) Dreschfeld, J.: Acute Disseminated Myelitis, *Brit. M. J.* 1:1174-1177, 1894. (m) Hoffman, J.: Ueber das Zusammenvorkommen von Sehnerven- und Rückenmarksentzündung, *Neurol. Centralbl.* 15:671-672, 1896. (n) Katz, K.: Ueber das Zusammenvorkommen von Neuritis optica und Myelitis acuta, *Arch. f. Ophth.* 42:202-240, 1896. (o) Taylor, F.: Myelitis and Optic Neuritis, *Guy's Hosp. Rep.* 53:45-54, 1896. (p) Schuster, P., and Bielschowsky, M.: Beitrag zur Pathologie und Histologie der multiple Sklerose, *Ztschr. f. Klin. Med.* 34:395-418, 1898. (q) Dalen, A.: Neuritis optica und Myelitis acuta, *Arch. f. Ophth.* 48:672-693, 1899. (r) Schuster, P., and Meindel, K.: Neuritis optica als Complication bei Erkrankungen des Nervensystems, *Neurol. Centralbl.* 18:1018-1023, 1899. (s) Taylor, J., and Collier, J.: The Occurrence of Optic Neuritis in Lesions of the Spinal Cord: Injury, Tumour, Myelitis: An Account of Twelve Cases and One Autopsy, *Brain* 24:532-554, 1901. (t) Faure, A.: De la neuromyéélite optique aiguë, *Thesis*, Lyons, no. 45, 1903, p. 66. (u) Weill, M., and Gallavardin, M.: Sur un cas de neuromyéélite optique aiguë, *Lyon méd.* 101:207-209, 1903; (v) Note sur l'anatomie pathologique de la myélite aiguë diffuse (myélites a cellules épithélioïdes), *Rev. neurol.* 11:999-1003, 1903. (w) Brissaud, E., and Brécy, N.: Neuromyéélite optique aiguë, *ibid.* 12:49-54, 1904. (x) Kerschensteiner, N.: Ueber Neuromyelitis optica, *Med. Wchnschr.* 53:802-805, 1906. (y) Hillion, H.: De la neuromyéélite optique aiguë, *Thesis*, Paris, no. 214, 1907, p. 160. (z) de Lapersonne, F.: La syndrome de la névrite optique associée a la myélite ophthalmoneuro-myéélitis, *Rev. neurol.* 21:378-381, 1911.

In 1927 the literature on neuromyelitis optica was again surveyed by Beck,<sup>12</sup> who found the diagnosis confused by the inclusion of coexistent myelitis and papillitis due to other causes; he noted that this combination may be seen in influenza, poliomyelitis, tumors and injuries of the cord, postencephalitic conditions and disturbances of lactation. Beck found multiple sclerosis and Schilder's disease most frequently confused with neuromyelitis optica. Including only those cases in which the principal symptoms were paraplegia and blindness, Beck<sup>13</sup> unearthed reports of 70 cases. According to his findings, the myelitis more often preceded the optic neuritis. Pathologic examinations were made in 25 of the cases in Beck's series; in 9 cases the lesions of the cord consisted of disseminated foci, while in 16 there was diffuse myelitis, varying in extent from 1½ inches (3.8 cm.) to nearly all the cervical, thoracic and lumbar segments. Beck suggested that these two pathologic types may represent two distinct diseases with a common clinical picture. His patient, a 15 year old girl, had four attacks of the disease, from three of which she made a complete recovery; then came a final loss of vision with a rapidly ascending paralysis that ended in blindness and death. Beck stated that the three remissions made his case unique; in his series he came across 7 instances of transient improvement for a few days, but no definite remissions such as these. Beck, too, concluded that neuromyelitis optica is a specific disease entity.

*English Literature Since 1927.*—There have been a number of case reports but no complete review of neuromyelitis optica in the ophthalmo-

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12. Beck, G. M.: A Case of Diffuse Myelitis Associated with Optic Neuritis, *Brain* **50**:687-703, 1927.

13. Beck reviewed the following articles, in addition to most of the works reviewed by Devic<sup>8</sup> and Goulden<sup>11</sup>: (a) Fürstner, N.: Zur Kenntniss der acuten disseminierten Myelitis, *Neurol. Centralbl.* **18**:155-161, 1899. (b) Ulrich, G.: Beobachtung von Opticuserkrankungen akuter genuiner Myelitis und Polyneuritis, *Ztschr. f. Augenh.* **29**:195-196, 1913. (c) Abelsdorf, G.: Akute retrobulbäre Sehnervenentzündung bei Myelitis mit Sektionsbefund, *Ztschr. f. Klin. Med.* **85**: 435-442, 1918. (d) Henneberg, G.: Ueber einem Fall von Myelitis cervicalis mit Opticuserkrankung und Brown-Séquardscher Lähmung, *Neurol. Centralbl.* **37**: 223-224, 1918. (e) Karplus, J. P.: Organische, nichttraumatische Nervenkrankheiten bei Kriegsteilnehmern, *Wien. med. Wchnschr.* **9**:137-148, 1919. (f) Buchanan, L.: Monocular Optic Neuritis, *Brit. J. Ophth.* **7**:170-174, 1923. (g) Jumentié, M. M., and Valière-Vialeix, V.: Sur un cas d'encéphalite aiguë non-suppurée de l'adulte avec névrite optique: Aspect ophtalmoscopique de stase papillaire; lésions à localisations prédominant sur le trajet des voies optiques intra et extra cérébrales, *Ann. d'ocul.* **162**:14-41, 1925. (h) Jendralski, F.: Die Entzündung des Sehnerven bei Myelitis acuta, *Klin. Monatsbl. f. Augenh.* **71**:19-28, 1923. (i) Genet, F., and Devic, C.: Neuromyéélite optique aiguë persistence anormale de séquelles neurologiques et oculaires, *Ann. d'ocul.* **162**:488-489, 1925. (j) Bouchut, L., and Dechaume, J.: Étude histopathologique d'un cas de neurooptico-myéélite aiguë, *Ann. d'anat. path.* **4**:357-372, 1927.



logic literature since 1927. In 1933 McAlpine<sup>14</sup> described a case in which the clinical diagnosis was disseminated sclerosis but at autopsy the diagnosis was changed to neuromyelitis optica. Cone, Russel and Harwood<sup>15</sup> reported a case in 1934 in which lead was demonstrated in the tissues of the brain and cord; they suggested this metal as the causative factor of the disease. Berliner<sup>16</sup> in 1935 discussed multiple sclerosis, acute disseminated encephalomyelitis, neuromyelitis optica and encephalitis periaxialis diffusa together as the demyelinating diseases of the nervous system and agreed with others that they may be variations of one entity, with clinical differences due to varying degrees of involvement or to predilection for special tissues. Walsh<sup>17</sup> in 1935 published the clinicopathologic study of a patient with neuromyelitis optica and the clinical histories of 3 other patients who survived. The first patient was a 9 year old girl who suffered blindness and ascending motor and sensory paralysis and died six weeks after the onset of the process. For 2 of the other patients an erroneous diagnosis of brain tumor was made and an exploratory operation performed, followed by almost immediate death. Walsh concluded that exploratory craniotomy or lumbar puncture in the demyelinating disease may cause an exacerbation of the process. In regard to specificity of Devic's syndrome, he concluded that his and similar cases are sufficiently distinctive clinically to warrant a special designation.

Balser<sup>18</sup> in 1936 discussed 3 cases of neuromyelitis optica pathologically and a fourth case clinically. Citing the work of Hurst,<sup>19</sup> Balser stated the opinion that it is unlikely that this disease is caused by a virus but he did concede the possibility in view of the small knowledge of virus diseases. He found remissions in a disease of such severity surprising. Hassin<sup>20</sup> published a case report in 1937 with a thorough pathologic study. He compared neuromyelitis optica with multiple sclerosis and disseminated encephalomyelitis and concluded that, although it might be impossible to differentiate these conditions clinically, it can be done microscopically. Fralik and

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14. McAlpine, D.: Myelitis with Blindness: Acute Disseminated Encephalomyelitis, *Proc. Roy. Soc. Med.* **27**:662-664, 1933-1934.

15. Cone, W. V.; Russel, C., and Harwood, R. U.: Lead as a Possible Cause of Multiple Sclerosis, *Arch. Neurol. & Psychiat.* **31**:236-269 (Feb.) 1934.

16. Berliner, M.: Acute Optic Neuritis in Demyelinating Diseases of the Nervous System, *Arch. Ophth.* **13**:83-98 (Jan.) 1935.

17. Walsh, F. B.: Neuromyelitis Optica, *Bull. Johns Hopkins Hosp.* **56**:183-210, 1935.

18. Balser, B. H.: Neuromyelitis Optica, *Brain* **59**:353-365, 1936.

19. Hurst, E. W.: The Neurotropic Virus Diseases: Wuthering Lecture of 1935, *Lancet* **2**:697-702, 1935.

20. Hassin, G. B.: Neuroptic Myelitis Versus Multiple Sclerosis: A Pathologic Study, *Arch. Neurol. & Psychiat.* **37**:1083-1099 (May) 1937.

DeJong,<sup>21</sup> in reporting the disease in a young lawyer, with acute loss of vision and an ascending spinal paralysis, progressing to death in six weeks, admitted the similarity of this process to multiple sclerosis, disseminated encephalomyelitis and diffuse sclerosis but stated that it could be differentiated clinically and pathologically from these other demyelinating diseases. Dolgopol<sup>22</sup> reported a case that was uncommon in two respects, namely, that the patient was a Negro and that she lived three years and eight months before succumbing to the disease.

McKee and McNaughton<sup>23</sup> described 2 cases in 1938, in both of which recovery occurred. One of their patients was followed for five years after recovery and visual acuity, visual fields and fundi remained normal. In addition to the usual signs and symptoms of visual and spinal involvement, McKee and McNaughton found that both their patients showed slight signs of invasion of the brain stem. In the discussion of their paper, Sanford Gifford<sup>24</sup> described 3 cases he had seen. He likened this syndrome to multiple sclerosis and said that in this condition one sees in a few short weeks what happens in multiple sclerosis over many years. Gifford raised the interesting speculation whether the patients who recover will later show signs of multiple sclerosis. Fatal neuromyelitis optica occurring in identical twin sisters was recorded by McAlpine<sup>25</sup> in 1938; 1 of the twins died of the disease at the age of 24 and the other at the age of 26 years. McAlpine collected 22 cases of this disease from the literature and divided them into three categories according to their clinical course: (1) cases which follow a progressive course with death in from five days to several weeks (10 cases); (2) cases which show one or more remissions but the patients finally die after several months (7 cases), (3) cases in which there is partial or complete recovery (5 cases).

In 1940 Fetterman and Chamberlain<sup>26</sup> reported a case of neuromyelitis optica in which there was complete recovery. These authors emphasized the necessity of careful differentiation between optic neuritis and papilledema from increased intracranial pressure. Although there are apparently striking clinical differences between Devic's disease and multiple sclerosis, Fetterman and Chamberlain suggested that the differ-

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21. Fralick, F. B., and DeJong, R. N.: Neuromyelitis Optica, *Am. J. Ophth.* **20**:1119-1124, 1937.

22. Dolgopol, V. B.: Neuromyelitis Optica, with Pathologic Study of a Case, *Arch. Neurol. & Psychiat.* **39**:561-569 (March) 1938.

23. McKee, S. H., and McNaughton, F. L.: Neuromyelitis Optica: A Report of Two Cases, *Am. J. Ophth.* **21**:130-137, 1938.

24. Gifford, S., in discussion on McKee and McNaughton,<sup>23</sup> p. 136.

25. McAlpine, D.: Familial Neuromyelitis Optica: Its Occurrence in Identical Twins, *Brain* **61**:430-448, 1938.

26. Fetterman, J. L., and Chamberlain, W. P., Jr.: Syndrome of Neuromyelitis Optica, *Arch. Ophth.* **23**:577-583 (March) 1940.

ence may be merely that of the time element, rather than of the etiologic agent or the pathologic picture. Because of the anatomic and physiologic complexity of the nervous system, the same etiologic agent may produce many different syndromes by pure chance of site and tempo of involvement; according to these writers, among the combinations of areas commonly affected (like 7 and 11 on the dice) are the optic nerves and spinal cord.

Utilizing the criteria laid down by Devic in 1894, Putnam and Forster<sup>27</sup> found 12 cases of neuromyelitis optica among the records of the Neurological Unit of the Boston City Hospital and the Neurological Institute of New York. The principal myelitic lesions corresponded to the description given by Devic, but there were, in addition, milder lesions scattered throughout the nervous system. Putnam and Forster attributed the cure in these cases to good treatment: tidal drainage for the cystitis and the Drinker respirator for respiratory failure. They followed 7 patients for six months or longer; 6 patients exhibited new neurologic manifestations and the condition became clearly recognizable as multiple sclerosis. They concluded, therefore, the Devic's syndrome is a subvariety of multiple sclerosis, except in a few bizarre and atypical cases.

In 1945 Kohut and Richter<sup>28</sup> reported 2 cases of neuromyelitis optica, 1 studied clinically and the other, with fatal outcome, with a complete work-up. Their pathologic description in the latter case is excellent. These authors favored the unicity of neuromyelitis optica, concerning which they said:

. . . the pathologic picture offered by the present case does not conform to even the broadest pathological conception of either multiple sclerosis or disseminated encephalomyelitis. Diffuse, massive necrosis of the spinal cord coupled with acute degeneration of the optic nerves, and complete absence of dissemination elsewhere in the central nervous system, constitute a pathological complex *sui generis*.

In the same year, Silbermann<sup>29</sup> contributed the history of a patient who lived, which was unusual in two respects: (1) The patient was a Negro, and (2) spinal block, substantiated by roentgenographic examination, occurred during the acute phase of the disease.

*French Literature.*—In 1930 Michaux,<sup>30</sup> studying under Guillain at the Salpêtrière, wrote an excellent doctoral thesis on neuromyelitis

27. Putnam, T. J., and Forster, F. M.: Neuromyelitis Optica: Its Relation to Multiple Sclerosis, *Tr. Am. Neurol. A.* **68**:20-25, 1942.

28. Kohut, H., and Richter, R. B.: Neur-Optic Myelitis: A Clinico-Pathological Study of Two Related Cases, *J. Nerv. & Ment. Dis.* **101**:99-114, 1945.

29. Silbermann, S. J.: Devic's Disease: A Clinical Review and Case Report, *J. Nerv. & Ment. Dis.* **102**:107-120, 1945.

30. Michaux, L.: La neuro-myélite optique aiguë, Thesis, Paris, Lousi Arnette, 1930, p. 289.

optica. He analyzed in detail his case and 21 cases from the literature.<sup>31</sup> Michaux attached no significance to the precedence of the visual or spinal disability; he said that chance determines which shall be first, or whether they come on simultaneously. Clinically, Michaux found neuromyelitis optica characterized chiefly by its variability; he could find no signs or symptoms that could be considered pathognomonic. He decried the fact that the cerebrospinal fluid had been examined in so few cases. Particularly good is Michaux's discussion of the differential diagnosis of this disease; he compared it with multiple sclerosis, cerebrospinal syphilis with optic neuritis, epidemic encephalitis, subacute necrotic myelitis, alcoholic polyneuritis, brain tumor and traumatic lesions of the cervical portion of the spinal cord. Admitting that only the demonstration of the causative agent will be decisive, Michaux concluded that, in the present state of affairs, neuromyelitis optica may be definitely distinguished from other diseases of the nervous system by its pathologic peculiarities.

Marinesco and colleagues<sup>32</sup> in 1930 discussed a fatal case of Devic's syndrome in which there were pathologic features common to both the latter disease and to Schilder's disease. Considering the rarity of lesions of the spinal cord in Schilder's disease and the comparative frequency of cerebral lesions in neuromyelitis optica, these authors classified their case as one of the latter. Milian and associates<sup>33</sup> stated

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31. Michaux reviewed the following reports: (a) Holden.<sup>60</sup> (b) Holmes.<sup>75</sup> (c) Goulden.<sup>10</sup> (d) Henneberg.<sup>13d</sup> (e) Abelsdorf.<sup>13c</sup> (f) Dollfuss, M. A.: Un cas de neuropticomyléite optique à évolution suraiguë, *Ann. d'ocul.* **163**:115-122, 1926. (g) Dechaume, J.: La neuropticomyléite aiguë: maladie à virus neurotrope; recherches expérimentales, Lyons, Edition du Service Photographique de l'Université de Lyon, 1926. (h) Euzière, P., and Bremond, R.: À propos d'un cas de neuropticomyléite, *Rev. d'oto-neuro-opht.* **5**:129-132, 1927. (i) Beck.<sup>12</sup> (j) Marinesco, G.: Un cas exceptionnel d'ophtalmo-neuro-myéite, *Rev. d'oto-neuro-opht.* **5**:379-380, 1927. (k) Vedel and Puech: Neuromyléite optique aiguë, *ibid.* **5**:125-128, 1927. (l) van Bogaert, L.: Neuro-myéite optique aiguë avec dissociation albuminocytologique du liquide céphalo-rachidien, *J. de neurol. et de psychiat.* **27**:106-107, 1927. (m) van Gehuchten, P., and Gaudissart, P.: Un cas de neuro-myéite optique: La stase papillaire dans les myélites; L'étiologie de la neuro-myéite, *Rev. d'oto-neuro-opht.* **5**:541-550, 1927. (n) van Gehuchten, M. P.: Deux cas de neuro-myéite optique, *J. de neurol. et de psychiat.* **27**:65-66 and 80, 1927. (o) Koelichen, M.: Cas de neuro-myéite optique à issue favorable, *Rev. neurol.* **2**:372-373, 1928. (p) Guillain, G.; Alajouanine, T.; Bertrand, I., and Garçin, R.: Sur une forme anatomo-clinique spéciale de neuro-myéite optique nécrotique aiguë avec crises toniques tétanoïdes: Contribution à l'étude des crises toniques sous-corticales, *Ann. méd.* **24**:24-57, 1928.

32. Marinesco, G.; Draganescu, S.; Sager, O., and Grigoresco, D.: Un cas anatomo-clinique d'ophtalmo-neuro-myéite: Sur les relations de cette affection avec la maladie de Schilder et la sclérose en plaques, *Rev. Neurol.* **54**:193-228, 1930.

33. Milian; Lhermitte; Schaeffer, and Horowitz: La neuropticomyléite aiguë: observation anatomo-clinique, *Rev. neurol.* **56**:257-279, 1931.

the opinion that neuromyelitis optica is a virus disease and attempted to isolate the virus in their case. They performed corneal scarification tests and intracerebral inoculations in monkeys and dogs with the cerebrospinal fluid. These investigators expected to find an unidentified neurocytotropic virus but were unsuccessful. Van Bogaert presented a case of neuromyelitis optica to the Paris Neurological Society in 1927<sup>31</sup>; in 1932 he<sup>34</sup> republished the case, after the death and autopsy of the patient, as multiple sclerosis. In van Bogaert's estimation, the original diagnosis was an error, the condition later proving to be multiple sclerosis. Ferraro<sup>35</sup> did not subscribe to van Bogaert's conclusion and offered this case as evidence of the difficulty in differential diagnosis of these two conditions. In 1934 Cestán, Riser and Planques<sup>36</sup> reported a case in which the typical lesions of neuromyelitis optica were associated with demyelination in the brain stem, cerebellum and cerebrum. Uréchia and Veluda<sup>37</sup> reported a case in which death occurred five days after the initial symptoms. In 1935 Alajouanine and associates<sup>38</sup> described lesions microscopically identical with those of multiple sclerosis in a case clinically typical of neuromyelitis optica; they concluded that these syndromes are part of the same disease. Kipfer<sup>39</sup> in 1945 presented a case with complete blindness that responded well to sulfonamide therapy; there was return of light perception in three days, regression of the myelitic symptoms in one week and almost complete cure of both in one year. Admitting the doubtful effect of the medication, Kipfer stated that the regression was so prompt and so spectacular that the case could not represent a coincidence of therapy and spontaneous remission.

*German Literature.*—In 1932 Kyrielleis<sup>40</sup> reported several cases of neuromyelitis optica; he expressed the belief that this disease repre-

34. van Bogaert, L.: Erreur de diagnostic: neuromyérite optique aiguë; premier stade d'une sclérose en plaque typique, *J. de neurol. et de psychiat.* **32**: 234-247, 1932.

35. Ferraro, A.: Primary Demyelinating Processes of the Central Nervous System: An Attempt at Unification and Classification, *Arch. Neurol. & Psychiat.* **37**:1100-1160 (May) 1937.

36. Cestán, Riser and Planques: De la neuro-myérite optiques, *Rev. neurol.* **62**:741-762, 1934.

37. Uréchia, C. I., and Veluda, P.: Neuromyérite optique aiguë avec controle anatomique, *Rev. neurol.* **61**:1039-1041, 1934.

38. Alajouanine, T.; Hornet, T.; Thurel, R., and Rossano, R.: Un cas anatomo-clinique de sclérose en plaques aiguë avec symptomatologie de neur-opticomyérite, *Rev. neurol.* **63**:98-109, 1935.

39. Kipfer, M.: Neuromyérite optique d'évolution suraiguë guérie après sulfamido thérapie intensive, *Rev. neurol.* **77**:151-153, 1945.

40. Kyriellis, W.: Ueber örtlich und zeitlich gehäuftes Auftreten von Neuritis nervi optici und Neuritis retro-bulbaris, sowie ihre Beziehungen zur Encephalomyelitis disseminata und zur multiplen Sklerose, *Deutsche Ztschr. f. Nervinh.* **124**:220-238, 1932.

sented an abortive form of multiple sclerosis and explained the clinical differences by postulating a variable intensity of the etiologic agent combined with a variable reaction in the patient. Klar<sup>41</sup> described 4 cases of this disease with severe monocular retrobulbar neuritis and total amaurosis, followed in a few days by the same process in the other eye. Klar inoculated the cerebrospinal fluid from his patients into the corneas of rabbits and produced superficial punctate keratitis. Ter Braak and van Herwaarden<sup>42</sup> in 1933 reported the ocular findings in 6 cases of neuromyelitis optica; their ocular findings consisted of (1) perivasculitis, (2) diffuse retinitis and (3) choroiditis. Popow<sup>43</sup> in 1935 reported a case of Devic's disease in which the blood culture was positive for staphylococci and the histologic examination of the spinal cord led to the diagnosis of purulent myelitis. Peters,<sup>44</sup> discussing 2 cases of this syndrome, differentiated neuromyelitis optica and multiple sclerosis on a pathologic basis. In 1936 Markiewicz and Peters<sup>45</sup> again stressed the difference in pathology in their presentation of 2 more cases.

*Other Reports.*—In the Italian literature, Salvati<sup>46</sup> reviewed the subject of neuromyelitis optica in 1931; he stated that the disease was an inflammation of the interstitial tissue of the nervous system. Gozzano<sup>47</sup> reviewed the literature again in 1937 and stated that the differences between neuromyelitis optica and multiple sclerosis are very great, although he considered them both virus diseases. In the Spanish literature, case reports have been published by Barcia Goyanes<sup>48</sup> and López Ibor.<sup>49</sup> In Russia, the disease has been reported by Shenderov,<sup>50</sup>

41. Klar, J.: Encephalomyelitis optica acuta, *Klin. Monatsbl. f. Augenh.* **89**:645-655, 1932.

42. ter Braak, J. W. G., and van Herwaarden, A.: Ophthalmo-Encephalo-Myelitis: encephalomyelitis disseminata mit ungewöhnlichen Augenerscheinungen, *Klin. Monatsbl. f. Augenh.* **91**:316-343, 1933.

43. Popow, N. A.: Neuromyelitis optica acuta, *Deutsche Ztschr. f. Nerven.* **135**:142-157, 1935.

44. Peters, G.: Zur Frage der Beziehungen zwischen der disseminierten, nichteitrigen Encephalomyelitis und der multiplen Sklerose, *Ztschr. f. d. ges. Neurol. u. Psychiat.* **153**:356-384, 1935.

45. Markiewicz, T., and Peters, G.: Beitrag, Klinik und Anatomie der Neuromyélie optique (Devic), *Ztschr. f. d. ges. Neurol. u. Psychiat.* **156**:287-301, 1936.

46. Salvati, G.: Neuromielite ottica, *Arch. ottal.* **38**:310-324, 1931.

47. Gozzano, M.: Sulla neuromielite ottica, *Riv. neurol.* **10**:529-573, 1937.

48. Barcia Goyanes, J. J.: Un nuevo caso de síndrome de Devic, *Crón. méd., Valencia* **37**:687-690, 1933.

49. López Ibor, J. J.: Neuromielitis óptica ambulatoria, *Crón. méd., Valencia* **37**:676-686, 1933.

50. Shenderov, L. A.: Neuromyelitis After Influenza, *Sovet. nevropat., psikhiat., i psikhogig.* **1**:639-645, 1932.

Ammasov<sup>51</sup> and Drombravskaya,<sup>52</sup> and in Turkey, by Mazal.<sup>53</sup> The first case of the disease diagnosed in China was described by Chang<sup>54</sup> in 1934. Recently, a case report by Stern<sup>55</sup> appeared in Palestine (1945), and by De and Chatterjee,<sup>56</sup> in India (1946).

NOTE.—Because of the limitations of space, no attempt has been made in this historical note to include all the papers and case reports on neuromyelitis optica. The number of publications on this rare disease is surprising. A supplementary list of references is appended to this paper, including many references prior to 1927 that were not listed in previous bibliographies.

#### REPORT OF CASES

CASE 1.—Mrs. S. S., a Negro woman aged 31, was admitted to the Neurological Institute on Jan. 18, 1936 because of numbness and weakness of the extremities and blurred vision in the left eye. The patient first noted the blurring of vision three weeks prior to admission. Four days before admission she noticed that her right thumb and the radial aspect of her right arm were "going to sleep." A few hours after this began, the entire right arm felt numb and weak; there was no pain. On the following day the numbness descended to the right leg, and by evening the entire right half of the body was numb and weak. Then the numbness appeared in the left foot and ascended to the knee. On the day of admission the patient observed the same symptoms in the fingers and palm of the left hand.

*Past History.*—The patient had the usual diseases of childhood. She had influenza in 1918, otitis media in 1928 and pneumonia in 1927. She had suffered from sinus trouble for three years. She had one child who was living and well; there had been but the one pregnancy. There was no history of familial disease. She was employed as a domestic. The remainder of the history was noncontributory.

*Physical Examination.*—The patient, a well developed young woman, exhibited difficulty in controlling the movements of her arms and hands, a bilateral wrist drop and an unsteady gait. The temperature, pulse, respiration and blood pressure were normal. Reflexes were hypoactive in the arms and hyperactive in the legs. A Babinski sign was elicited bilaterally, and abdominal reflexes were absent on the left. The pupillary reaction to light was sluggish, and there was questionable pallor of the left optic disk. Sensory examination showed hypesthesia over both upper and lower extremities. Position sense was impaired in the arms, and vibratory sense was lost in the legs. Pain and temperature sensations were diminished on the right side, with patchy involvement on the left. Physical examination revealed nothing else abnormal except for kyphoscoliosis.

51. Ammasov, M. M.: Clinical Aspects and Pathologic Anatomy of Neuro-myelitis Optica, *Sovet. psikhonevrol.*, no. 3, 5-14, 1936.

52. Drombravskaya, R. I.: Optic Encephalitis, *Klin. med.* **19**:50-55, 1941.

53. Mazal, V.: Case of Optic Neuromyelitis, *Časop, lék. česk.* **72**:952-954, 1933.

54. Chang, S. P.: Acute Retrobulbar Neuritis in Myelitis: Report of a Case, *Chinese M. J.* **48**:991-998, 1934.

55. Stern, A.: Acute Multiple Sclerosis with Symptomatology of Optic Neuromyelitis, *Harefuah* **29**:236-237, 1945.

56. De, M. N., and Chatterjee, J. R.: A Case of Neuromyelitis Optica, *Indian M. Gaz.* **81**:361-362, 1946.

*Ophthalmologic Consultation* (Jan. 25, 1936).—Vision was 20/20 in the right eye and 20/200 in the left eye. Externally, the eyes were normal. The anterior chamber and media were clear in both eyes. The pupillary reflexes in the right eye were normal; the pupil in the left eye was sluggish, and its excursion was only half that of the right eye. The fundus was normal in the right eye, but the optic disk on the left showed primary optic nerve atrophy. The peripheral fields were within normal limits. The impression was stated that there is nothing in the eyegrounds to indicate an acute process; on the contrary, the fundus on the left appeared to be an old process.

January 27: Another ophthalmologist saw the patient and found a large central scotoma in the left eye. He described the left optic disk as showing moderate temporal pallor. The impression was that of "recent retrobulbar neuritis of the left eye, most likely caused by whatever had produced the other neurologic changes."

March 4: The central fields showed a large centrocecal scotoma on the left (fig. 1); the peripheral fields were normal.

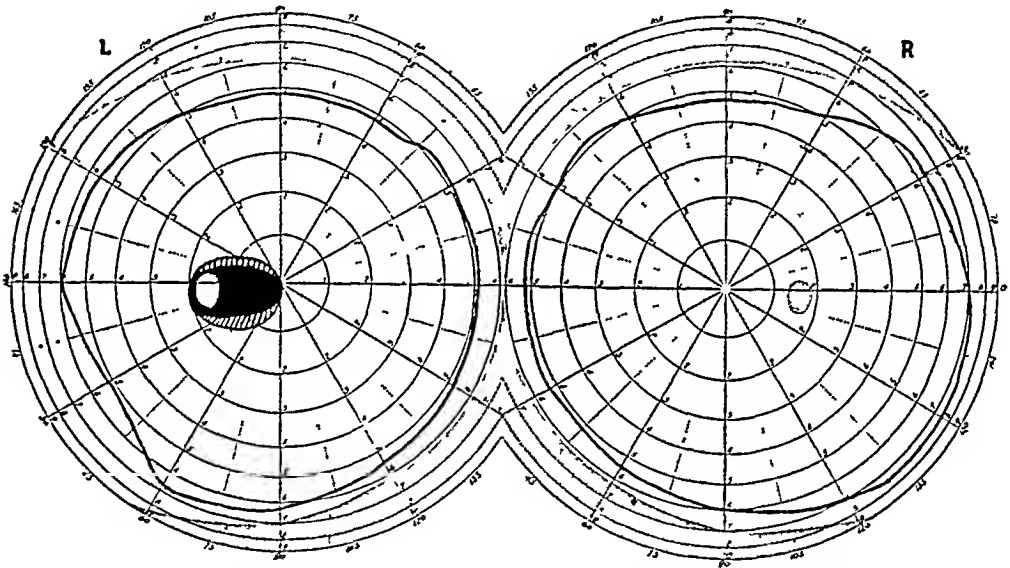


Fig. 1 (case 1).—Central fields on March 4, 1936. The cross patched areas show scotoma for 1 mm. red test object; the black area, scotoma for 2 mm. white test object.

*Laboratory Findings.*—The blood count was normal until near the patient's death, when the white cell count was 13,000, with a normal differential distribution. The Wassermann reaction was negative on all occasions. Repeated examinations of the urine revealed few to many white cells, an acid reaction, normal specific gravity and no sugar or acetone. Examination of the spinal fluid on four occasions, with approximately the same results, disclosed a clear fluid; normal dynamics; 10 cells per cubic millimeter; a 1 plus reaction for globulin; 56 mg. of protein, 62 mg. of sugar and 702 mg. of chlorides, per hundred cubic centimeters, a negative Wassermann reaction and a colloidal gold curve of 1233332100 on two occasions. All other laboratory findings were normal.

*Course.*—It was the impression of the staff that the patient had an acute intrinsic disease of the central nervous system, either neuromyelitis optica or neurosyphilis. Provocative Wassermann tests were done, with negative reactions of both the blood and the spinal fluid. The patient's symptoms and neurologic status changed from day to day, and the findings varied with different examiners.



On January 30, urinary retention developed, necessitating catheterization. Her urinary difficulty cleared up, only to recur in a few weeks. Spinal drainage was performed, without benefit. Paralysis of the extremities was progressive and became severe in all four limbs. The sensory disturbances progressed until all sensory functions were abnormal to the third cervical segment. She complained of excessive perspiration about the head and neck and had episodes of hiccups. Motor function returned temporarily to a considerable degree on the right side. On the other hand, there developed profound motor palsies in the left arm and leg, which were severer than were ever noted on the right. No spasticity was seen; instead, hypotonicity was the rule. The patient became stuporous the day before her death. Respiration became rapid and shallow; then just before death, extremely slow, and finally imperceptible. She died March 9, approximately two and a half months after the onset of her visual difficulty.

*Clinical Diagnosis.*—The clinical diagnosis was encephalomyelitis.

*Autopsy.*<sup>57</sup>—*Macroscopic Observations:* External examination of the body revealed nothing remarkable. Internally, the body cavities and the enclosed viscera appeared normal. The brain, cerebellum, brain stem and spinal cord appeared (autopsy of the nervous system) grossly normal. On section, the cervical portions of the spinal cord revealed indistinct margins between the white and the gray matter and a yellowish gray discoloration of the posterior columns and the left lateral column. There were similar lesions in the upper half of the thoracic portion of the cord.

*Microscopic Observations:* The abdominal and thoracic organs all appeared normal except the lungs, which showed a typical picture of active bronchopneumonia.

*Brain and brain stem.* The cerebrum showed congestion and edema and some diffuse loss of ganglion cells in the cortex, but no other changes of note. The brain stem was congested and contained occasional small perivascular hemorrhages. The pia of the medulla was infiltrated with lymphocytes and plasma cells, and the parenchyma of the medulla was congested. The Marchi stain of the lower part of the medulla showed scattered foci of degeneration, and the Weigert stain revealed occasional small foci of demyelination. These areas were edematous, and the ganglion cells were pale and partially degenerated. There was some microglial proliferation. The pons showed occasional perivascular infiltrations and hemorrhages.

*Optic nerves.* Hematoxylin and eosin stains of the left optic nerve revealed homogeneous, pale pink interstitial tissue between the nerve bundles, with little of the normal architecture remaining. These spaces were rich in microglia cells and hypertrophied astrocytes; the microglia cells were seen in all stages of transition, from rod cells to gutter cells. The microglia cells were most numerous within the degenerated areas, while the astrocytes were commoner at the margins of these areas. There was extensive perivascular infiltration of lymphocytes and plasma cells, both in the nerve substance and in its meninges. With phosphotungstic acid stains, the astrocytes were especially well demonstrated. The Spielmeyer and Weigert stains showed these areas to be extensively demyelinated. The Bodian stain demonstrated a decrease in the number of axons and severe pathologic changes in the remaining fibers, which were poorly stained, fragmented and very irregular in caliber. The presence of neutral fat shown with the Marchi stain demonstrated that the process was comparatively recent, and probably still active. There was no evidence of hyperplasia of glial fibers.

57. Autopsies of the nervous system in this case and in the other cases reported were performed by Dr. Abner Wolfe.

The right optic nerve showed changes similar to those in the left nerve, but of considerably milder degree. (There was no clinical evidence of involvement of this nerve.) Figure 2 is a photograph of a Weigert stain of the two nerves. The optic chiasm showed the same diffuse demyelination, which was again severer

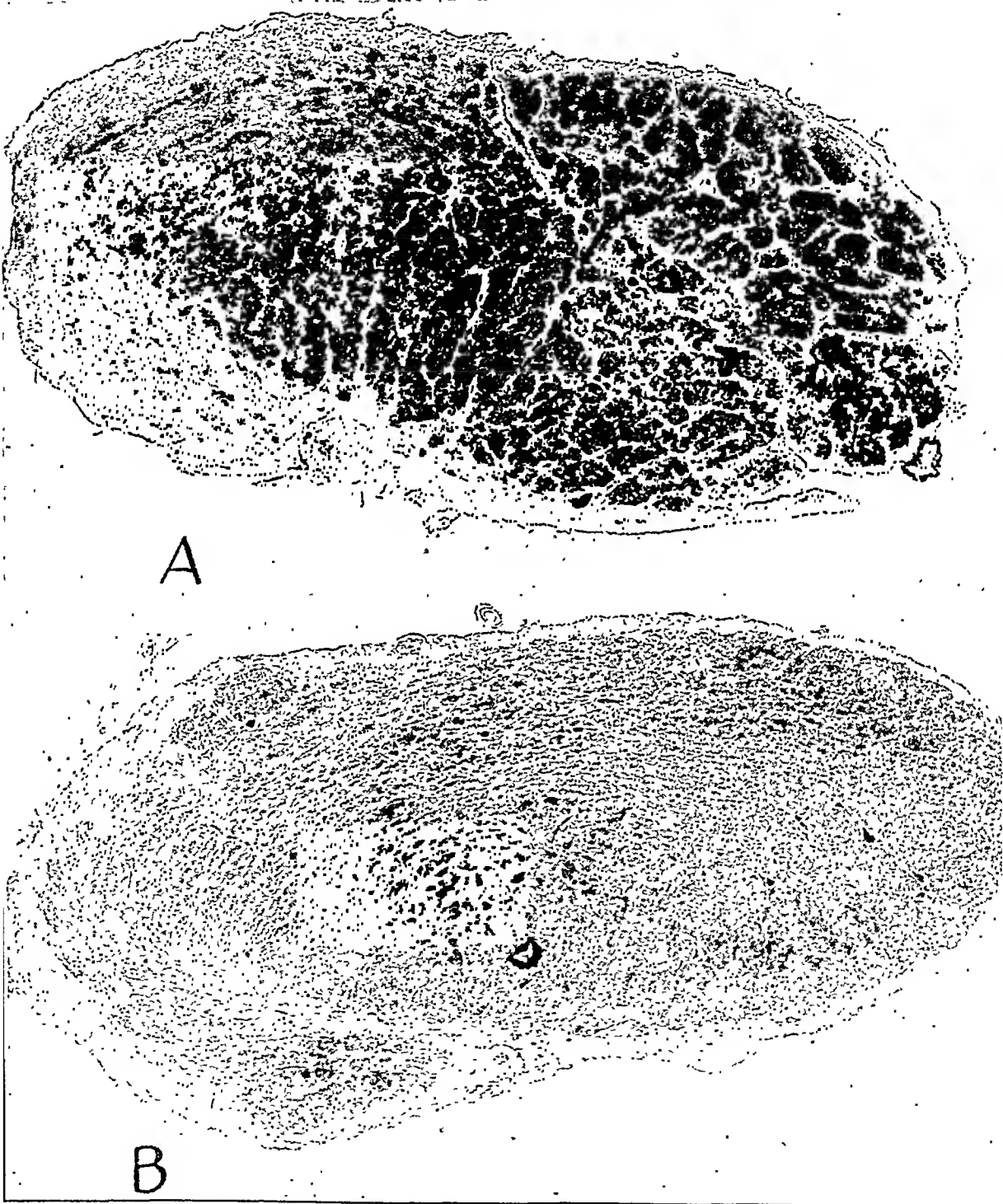


Fig. 2 (case 1).—Weigert stains of the optic nerves. (A) The right optic nerve appears grossly almost normal but microscopically shows slight diffuse demyelination. (B) The left nerve shows extensive demyelination of the entire cross section, although severer in some areas than others.

on the left side. The fibers from the left optic nerve which enter into the decussation are seen to be almost entirely devoid of myelin sheaths.

Spinal cord. The hematoxylin and eosin stains show diffuse infiltration of the leptomeninges with lymphocytes and plasma cells. A similar infiltration was seen about the blood vessels entering the parenchyma of the cord from the surface. In the cervical sections, the greater part of all the white columns was undergoing intense degeneration. In the thoracic segments, there was advanced degeneration of the periphery of the posterior and lateral white columns and parts of the anterior columns. In addition to these more extensive lesions, there were many minute foci throughout the remaining white matter and pronounced necrosis of the central gray substance.

Histologically, these areas proved to be foci of softening or necrosis, with loss of axons, myelin sheaths and neuroglia. Within these areas there were many compound granule cells, as well as a multiplication of microglia cells, many of which were in the process of conversion to compound granule cells. In general, the outer edge of the necrotic band was broken down and edematous, while its inner aspect showed greater infiltration and progression of the process. Partially degenerated zones were seen, containing bright red fragments of swollen axons, degenerating astrocytes, proliferating microglia cells and developing compound granule cells. Occasional corpora amylacea were seen developing from degenerated astrocytes. In the more severely affected foci, fragmentation of fibers and clasmotodendrosis of the astrocytes were seen. The phosphotungstic acid hematoxylin stain revealed that many of the astrocytes near the margins of the degenerated zones were hypertrophied; within the zones they were partially or completely necrotic. The Spielmeyer stain revealed demyelination of the areas just described, with swelling and fragmentation of myelin sheaths in the less severely affected areas. Frequently the smaller areas of demyelination were observed to be perivascular, and these could be seen to coalesce into the larger lesions. With the Marchi stain, irregular areas of degeneration were observed in all the white columns. There was intense congestion and edema, as well as some necrosis in the anterior and posterior gray horns. Many of the nerve cells of the anterior horn were undergoing degeneration; these were deformed, lacking in their Nissl substance, pale staining, filled with an excess of lipid and occasionally vacuolated. There was some multiplication of microglia cells here as well. There were also foci of demyelination in the anterior and posterior roots.

The lumbar and sacral segments were only minimally involved. The dorsal ganglions showed mild infiltration of lymphocytes and plasma cells. Some of the ganglion cells were vacuolated and laden with lipid. With the phosphotungstic acid hematoxylin stain, some of the axons in the roots appeared irregularly swollen. With the Weigert stain sections of the right sciatic nerve showed occasional degenerated myelin sheaths. There was Marchi degeneration of scattered sheaths in each bundle of this nerve. With the Weigert stain the left brachial nerve showed even more degeneration than did the sciatic nerve.

*Anatomic Diagnosis.*—The anatomic diagnosis was neuromyelitis optica.

*Summary.*—The patient, a young Negro woman, had blurred vision of the left eye and numbness and weakness in the arms and legs. Examination on her admission revealed an unsteady gait, ataxia, hyporeflexia in the arms and hyperreflexia in the legs, with a bilateral Babinski sign. She had mild pallor of the left optic disk and a central scotoma. Sensation was impaired throughout. The spinal fluid was normal except for the presence of a small amount of globulin. There was evidence of disseminated lesions in the central nervous system, and the diagnosis

rested between neuromyelitis optica and neurosyphilis. The course was progressive, although the symptoms varied from day to day. The patient finally became stuporous and died two and a half months after the onset of her visual difficulty.

Autopsy revealed diffuse demyelination of both optic nerves, although there was no clinical evidence of damage to the right nerve. In the spinal cord, advanced necrosis was present throughout the thoracic and cervical levels. Intense demyelination was noted in the white columns; the demyelination was irregular, not involving any definite systems. The lesions did not appear to be essentially perivascular, although they might have been the result of coalescence of perivascular foci. There were intense multiplication of the microglia cells and conversion into fat granule cells. There was extensive perivascular infiltration of lymphocytes, plasma cells and monocytes. Pathologically, this case must be considered one of disseminated encephalomyelitis, of the type known as "optic neuromyelitis."

CASE 2 (presented with the permission of Dr. Gordon M. Bruce).—W. E., a white man aged 57, a carpenter, was referred to Dr. Gordon M. Bruce, on July 1, 1938, with a history of blurred vision for three weeks. The patient had had good health and good vision until March 1938, when he began to have pains behind the eyes. After a change in glasses by his local oculist the pains gradually ceased. Early in June he noticed blurring of vision of the left eye and, after a few days, in the right eye. On June 20 he became conscious of numbness of the face, which he attributed to the extraction of teeth. The patient's family history was not unusual, and his past history revealed only the usual diseases of childhood, a history of hay fever for twenty-five years and allergy to bananas and cheese.

*Ophthalmologic Examination* (July 1).—Visual acuity was 20/40 in the right eye, and 1/200 in the left eye; there was no improvement with glasses. Externally, the eyes appeared normal. The pupils were round, equal and active. Tension was normal in both eyes. Ophthalmoscopic study revealed a small area of old chororetinitis in the periphery of the right eye; otherwise the fundi were normal. The peripheral fields were normal. The tangent screen revealed enlargement of the blindspot on the right and a very large central scotoma, involving the blindspot, on the left (fig. 3A). Roentgenograms of the orbits were normal. A diagnosis of acute retrobulbar neuritis was made, and the patient was admitted to the Institute of Ophthalmology for study.

*Physical Examination*.—The patient, an elderly white man, did not seem acutely ill. The temperature, pulse, respiration and blood pressure were normal. He possessed many carious teeth. His heart was slightly enlarged to the left, but physical examination was otherwise noncontributory. Neurologic examination gave normal findings except for a positive reaction to the Romberg test.

*Laboratory Findings*.—The blood count showed 16,700 white cells, with 89 per cent polymorphonuclear leukocytes, 9 per cent lymphocytes and 2 per cent monocytes. The sedimentation rate was 30 mm. per hour. The urine was normal, and the Wassermann reaction of the blood was negative. Roentgenograms of the chest and skull were normal. Examination of the spinal fluid revealed clear fluid; normal dynamics; no cells; a positive reaction of the Pandy test; 59.5 mg. of protein, 95 mg. of sugar and 681 mg. of chlorides, per hundred cubic cen-

timeters; a colloidal gold curve of 1111100000, and a negative Wassermann reaction. All other laboratory findings were within normal limits.

*Course.*—With hospitalization, vision improved in the left eye; at the same time, it decreased rapidly in the right eye. The central fields on July 15 showed shrinkage of the central defect on the left and a new large centrocecal scotoma on the right (fig. 3*B*). Vision was not tested at this time. Neurologic consultation disclosed staggering with a wide base; a positive Romberg sign; poor

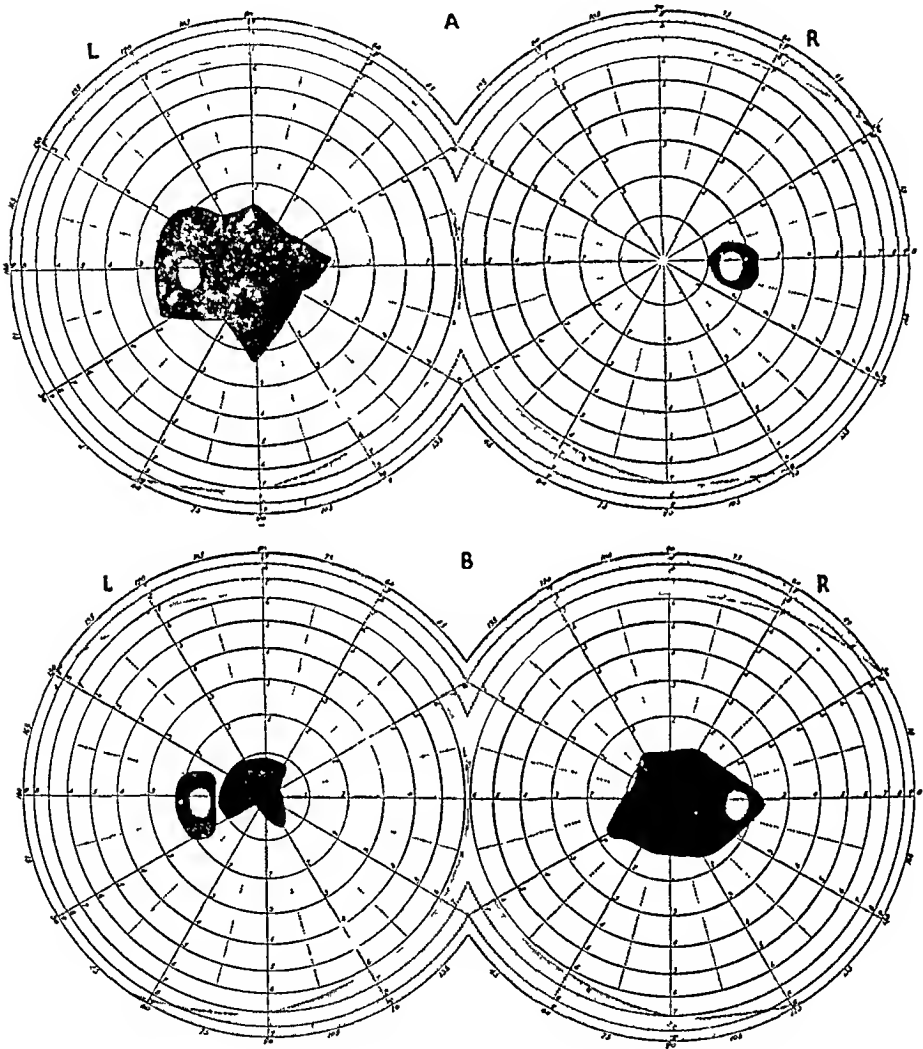


Fig. 3 (case 2).—*A*, central fields taken on July 1, 1938, showing enlargement of the blindspot of the right eye and a large centrocecal scotoma on the left (3 mm. white). Corrected vision was 20/40 in the right eye and 1/200 in the left eye. *B*, central fields on July 15, showing shrinkage of the central defect of the left eye, and a new large centrocecal scotoma on the right (3 mm. white). These fields are reproduced by courtesy of Dr. Gordon M. Bruce.

coordination; hyperreflexia, more pronounced on the right side; weakness of all four extremities; and normal sensation. The neurologic consultant discarded multiple sclerosis as a diagnosis because of the patient's age and suggested an allergic process, causing focal edema in the optic nerves and cerebellar pathways

The patient was placed on a vigorous dehydration program but failed to improve. His neurologic symptoms gradually became more pronounced, and he fell several times when trying to walk alone. On July 20 he was transferred to the Neurological Institute, unimproved.

On July 21 the patient complained of a tingling sensation in his arms and legs; this was most pronounced in the hands and feet, extending up the arms to the elbows and up the legs to the knees. He also noticed a noise in his ears, not associated with any diminution in hearing. The next day he complained of great dizziness. Examination on July 26 revealed increased staggering; marked ataxia; increased muscular weakness of the extremities; hyperreflexia; questionable blurring of the optic disks; irregular jerky nystagmus on lateral gaze; reduced pharyngeal reflex, and a deviation of the uvula to the left. Vision was then 20/200 in each eye. His condition grew rapidly worse, and he began to exhibit signs of respiratory embarrassment. He died on July 31, with respiratory failure. The

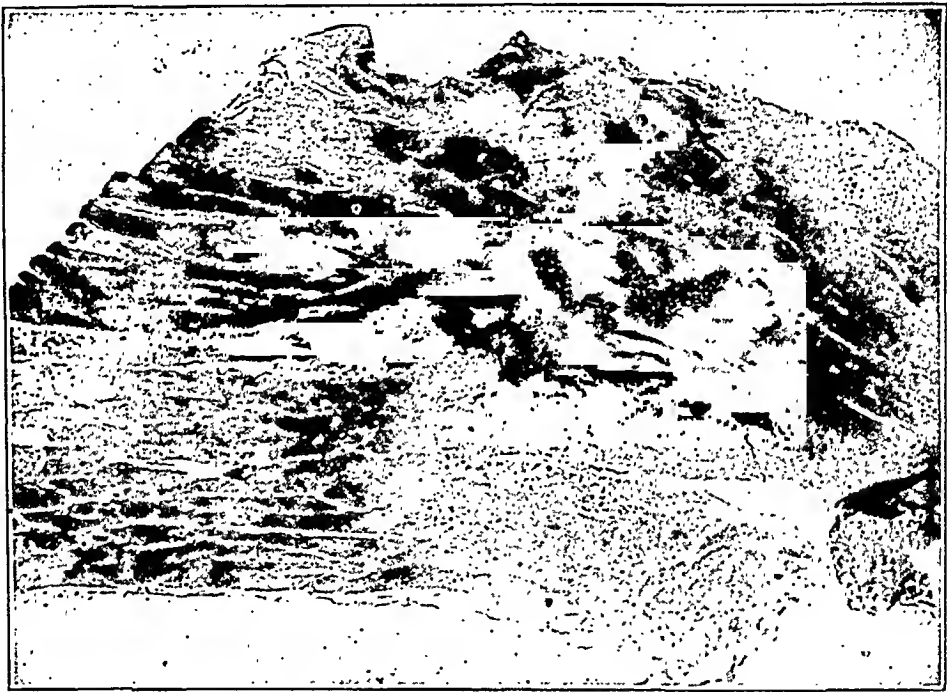


Fig. 4 (case 2).—Smith-Quigley stain of the right optic nerve, showing a number of small foci of demyelination and one large coalescent focus below.

patient showed such a multiplicity of neurologic symptoms and signs that it was impossible to explain them on the basis of any single lesion in the central nervous system.

*Clinical Diagnosis.*—The clinical diagnosis was encephalomyelitis.

*Autopsy.*—*Macroscopic Observations:* Externally, there was only mild wasting of the muscles of the arms and hands. (Permission limited the examination to the brain and spinal cord.) The brain, cerebellum, brain stem and spinal cord appeared normal externally and on cut section.

*Microscopic Observations:* Brain and brain stem. The leptomeninges were congested and contained occasional petechial hemorrhages and scattered collections of lymphocytes. Many of the nerve cells of the cerebrum were pale staining and showed chromatolysis. The Pal-Weigert stain revealed no demyelination of these tissues.

**Optic nerves.** With the hematoxylin and eosin stain, the optic nerves showed coalescent areas of necrosis with infiltration by polymorphonuclear leukocytes, lymphocytes and monocytes. In these areas there were edema, destruction of the neural elements, conversion of microglia into fat granule bodies, degeneration of astrocytes and oligodendrocytes and proliferation of capillaries. Lipid-laden phagocytes were packed in the perivascular spaces and lymphocytic masses were seen around the blood vessels. In the more severely involved foci, there were a loss of architectural markings and more abundant perivascular exudate. The Smith-Quigley stain showed small discrete and large coalescent areas of demyelination (fig. 4); in these necrotic foci a few poorly preserved myelin sheaths were still present. With the phosphotungstic acid hematoxylin stain, sections of both nerves showed pronounced astrocytosis.

**Pons.** The meninges were infiltrated and congested, as already noted. Many of the vessels penetrating the parenchyma from the meninges showed similar perivascular infiltration of lymphocytes and plasma cells. A number of large necrotic lesions affected most of the structures of the reticular portion of the pons and a single large lesion involved the center of one-half the tegmentum. These lesions showed edema, necrosis and degeneration of the tissues, similar to the lesions in the optic nerves. There was conversion of microglia into lipid-scavenging phagocytes throughout the sections. There were fragmentation and destruction of the interstitial tissue. The nerve cells in the nuclei outside the lesions contained excessive lipid material, and some were partially destroyed. The Pal-Weigert stain demonstrated intense demyelination of the lesions previously described (fig. 5), although small numbers of preserved myelin sheaths were seen to pass through the softened areas. At the margins of these areas myelin sheaths were undergoing fragmentation and degeneration, showing that the lesions were still active. Some of the demyelinated areas were sharply demarcated, particularly the one in the tegmentum, but many of those in the reticular area were confluent. The Cajal stain showed small numbers of hypertrophied astrocytes about the margins of these lesions.

**Spinal cord.** The meninges and parenchyma were congested, and many of the anterior horn cells showed excessive lipid material. There were no other changes of note.

*Anatomic Diagnosis.*—The anatomic diagnosis was neuromyelitis optica.

*Summary.*—A middle-aged man suffered sudden retrobulbar pain for a few days, followed in three months by blurring of vision. He began to have difficulty in walking, staggering but not falling. There then developed a varied assortment of motor, sensory and cranial nerve symptoms and signs, and the patient eventually died of respiratory failure, four months after the onset of visual difficulty.

Autopsy revealed acute necrotic perivascular lesions in the pons and optic nerves. Microscopically, the main features were demyelination, destruction of axons, proliferation of astrocytes, proliferation and conversion of microglia into fat-scavenging phagocytes and perivascular infiltration of lymphocytes, monocytes and plasma cells.

The pathologic and clinical pictures are those of neuromyelitis optica, but the process was observed only in the optic nerves and pons. The absence of lesions in the spinal cord was unusual. In view of the fact

that the lesions in the spinal cord in neuromyelitis optica may be confined to a few segments, one might consider this an analogous state, in which the pathologic lesions were confined to the brain stem instead.

CASE 3.—Miss L. J., an 18 year old Jewish girl, had onset of weakness of the left arm and leg on April 1, 1941. On April 10 she noticed clumsiness of the left hand and numbness of the left side of the body. These disabilities were



Fig. 5 (case 2).—Pal-Weigert stain of the pons, showing extensive areas of severe demyelination.

progressive, and her gait became unsteady. Blurring of vision was first noted on April 20. She became euphoric and confused. On April 24 she was admitted to the Neurological Institute for study.

*Physical Examination.*—The patient, a well developed girl, appeared drowsy and somnolent. The temperature, pulse, respiration and blood pressure were normal. Neurologic examination revealed weakness of the legs, with inability



to stand alone; slight pallor of the optic disks; equal and symmetric pupils, which reacted to light and in accommodation; poor convergence; defective conjugate movements of the eyes, anesthesia of the trigeminal nerve on the left; weakness of the left side of the face; protrusion of the tongue to the right; poor coordination; slurring of speech; a positive Babinski sign on the right, and normal sensation over the body. The remainder of the physical examination showed nothing abnormal.

*Laboratory Findings.*—The blood count showed leukocytosis, with a count of 16,450 with 89 per cent polymorphonuclear leukocytes, 9 per cent lymphocytes, 1 per cent monocytes and 1 per cent eosinophils. The urine was normal. Examination of the spinal fluid revealed clear fluid; normal dynamics; 9 white blood cells per cubic millimeter; 68 mg. of protein and 65 mg. of sugar per hundred cubic centimeters; a colloidal gold curve of 1100000000, and a negative Wassermann reaction. All other laboratory findings were within normal limits.

*Course.*—On April 26 weakness of the right arm and leg developed. She was confused, forgetful and euphoric most of the time. The Babinski reflex was elicited bilaterally, and sensation was lost over the left side of the body below the fourth thoracic segment. On April 30 she was disoriented as to time and place. The pupils were large, equal and symmetric and reacted poorly to light. She could not converge her eyes, and there was paralysis of upward gaze. Sensory loss over the right side of the face developed. Deep reflexes were hyperactive in the right arm and the left leg, and the abdominal reflexes were lost. Poor vision developed bilaterally (it was normal before admission, according to her family physician), but study of the fundus revealed no abnormality. (Visual acuity was not determined.) One examiner noted normal excursions of the right eye, with limitation of motility of the left eye in all directions; he also noted left homonymous hemianopsia. On May 1 the patient lapsed into coma and became incontinent of feces and urine. On May 3 the pupils were widely dilated, with no reaction to light or convergence; there were paralyzes of the third and sixth nerves bilaterally. At this time she showed left hemiplegia, with a spastic arm and a flaccid leg; there was right hemiparesis, severer in the leg. On May 4 the patient had complete bilateral ophthalmoplegia, and the fundi still appeared normal. She slowly became more somnolent and exhibited a tendency toward decerebrate posture. Her temperature began to rise; respiration became slower, and the pulse became slow and indistinct. She died on May 13 of respiratory paralysis, six weeks after the onset of motor and sensory symptoms.

*Clinical Diagnosis.*—The diagnosis was encephalomyelitis.

*Autopsy.*—Macroscopic Observation: External examination was noncontributory. Internally, the body cavities and enclosed viscera were within normal limits. Grossly, the brain, cerebellum, brain stem and spinal cord appeared normal. On section of the cerebrum, the centrum ovale on each side contained numbers of sharply demarcated lesions, which were salmon colored and studded with yellow punctate areas. Section of the brain stem revealed a pyriform lesion in the right cerebral peduncle. The pons also contained several small lesions. The upper cervical segments of the spinal cord showed a wedge-shaped lesion in the right lateral white column. There were scattered small lesions through the rest of the cervical portion of cord and in the sections of the lumbar portion of the cord, but no lesions were seen in the thoracic segments.

*Microscopic Observations:* The sections of the thoracic and abdominal viscera were within normal limits.

Cerebral cortex. There were many lesions in the subcortical white matter; the smallest of these were perivascular. Often, however, these perivascular lesions coalesced into larger lesions, so that the appearance was that of an irregular patch of softened white matter, which was edematous and diffusely infiltrated with lipid-laden phagocytes and small numbers of lymphocytes. There was degeneration of all the neural elements in these patches, with destruction of myelin sheaths, axons and neuroglia. The Mahon stain demonstrated nearly complete loss of myelin sheaths within these lesions, although fragments of myelin of varying size were seen at the margins of the foci. The Bodian stain disclosed the preservation of some axons, even in the areas with the greatest necrosis; these remaining axis-cylinders occasionally showed swelling and fragmentation. With the Nissl stain, occasional cells showed loss of Nissl substance. Moderate astrocytosis was revealed by the phosphotungstic acid hematoxylin stain but appeared more prominent than it actually was because of the size attained by these hypertrophied astrocytes.

Centrum ovale: Lesions similar to those just described were also noted in this area. The Mahon stain showed extensive demyelination, which was perivascular, although some large, coalesced lesions could be seen.

Midbrain. The substantia nigra and the cerebral peduncle on one side contained a large, coalesced lesion. There were another lesion just lateral to the aqueduct of Sylvius and a few small scattered lesions. The Mahon stain showed total demyelination in these foci. With the Bodian stain, the discrepancy between the loss of axons and the myelin sheaths is more striking here than in any of the preceding sections.

Pons. Large, irregular lesions were present in the reticular zone, and a number of small foci were seen in the tegmentum. There was intense demyelination in all these lesions. The pictures with the Bodian, phosphotungstic acid hematoxylin and Nissl stains were similar to those already described.

Medulla. Small lesions, similar to those in the pons, were scattered throughout the medulla.

Spinal cord. At the cervical level, there was a large, coalescent lesion in the lateral and anterior white columns, surrounding and involving a portion of one anterior gray horn (fig. 6). In addition, there were numerous small lesions in the marginal white matter. A large, wedge-shaped lesion, similar to that seen in the cervical segments, was also noted in the thoracic sections. At the lumbar level large lesions were present in all but the posterior white columns; occasional small lesions were also seen. Both the anterior and the posterior gray horn were involved in large lesions. The microscopic changes were essentially similar to those described in the cerebrum; some of the nerve cells in the anterior gray horns were, unexpectedly, well preserved.

Optic nerves. There were a number of areas of perivascular infiltration in the connective tissue trabeculae of the right optic nerve associated with microglial proliferation within the nerve bundles. The Mahon stain showed perivascular demyelination in these foci (fig. 7); myelin fragments were still present within the lesions. With the Bodian stain the axons appeared separated and decreased in number within the lesions; none of them appeared swollen or fragmented. A mild astrocytosis was apparent with the phosphotungstic acid hematoxylin stain. The left optic nerve appeared normal.

*Anatomic Diagnosis.*—The diagnosis was neuromyelitis optica.

*Summary.*—An 18 year old girl had onset of weakness and numbness of the left side of the body, followed by unsteadiness of gait and

blurring of vision. She became euphoric and confused and then somnolent. The paresis became paralysis and attacked the right side, as did the sensory loss. Her vision became poor, and complete ophthalmoplegia developed. Finally, after six weeks, she became comatose and incontinent and died. Autopsy revealed disseminated foci of necrosis and demyelination in the cerebrum, brain stem, spinal cord and optic nerves. There was destruction of all neural elements, with abundant microglial phagocytosis and moderate astrocytosis. There was considerably more involvement of the brain and the brain stem in this case than in the typical case of neuromyelitis optica.



Fig. 6 (case 3).—Mahon stain of a section of the cervical portion of the spinal cord, showing a large lesion involving the lateral and anterior white columns on one side and impinging on the anterior gray horn adjacent.

CASE 4.—M. W., a white housewife aged 29, was admitted to the Neurological Institute on Sept. 29, 1945, with the complaints of (1) paralysis of the left leg and weakness of the right leg, (2) numbness on both sides up to the nipple line, (3) urinary and fecal retention and (4) pain in both shoulder girdles. About a week before admission, the patient noticed burning sensations over the abdomen and legs, with sensitivity to touch in the affected areas. She also noted intermittent jerking of the left foot; this involuntary motion continued for about two minutes at a time. She then became aware of numbness in the left foot, which soon appeared in the right foot and progressed up both legs, so that in three days the numbness extended to her breasts. Her legs became so weak that she could not walk, and then she could not move her left leg at all. Urinary retention and constipation developed. Two days before admission pains developed

in her shoulders, neck and back. Tingling, numbness and a cold sensation then appeared in both arms and was beginning to involve the hands at the time of her entrance to the hospital.

*Past History.*—Two years prior to admission the patient suddenly became blind in the right eye, during an episode of abscessed teeth. The teeth were removed, and two months later her vision return to normal. In October 1944 she was hospitalized for pain in the back and abdomen, associated with constipation. A diagnosis of an acute abdominal condition was made, and an exploratory laparotomy was performed. The appendix and a cyst of the left ovary were removed, and the uterus was found to be enlarged to the size characteristic of a ten weeks' gestation. After operation the patient experienced progressive weakness of both legs, with areflexia and normal sensation. The spinal fluid appeared



Fig. 7 (case 3).—Mahon stain of a section of the right optic nerve, showing a number of foci of demyelination.

normal on examination. A diagnosis of poliomyelitis was made, and she received the Sister Kenny treatment. In January 1945, with physical therapy, she began to show some improvement in muscular power. In April 1945 she was delivered of a normal child, and in May she was able to walk with crutches. She was discharged from the hospital, with residual weakness of the muscles of the abdomen, back and left thigh.

*Physical Examination.*—The patient appeared ill and anxious. The temperature, pulse, respiration and blood pressure were normal. Neurologic examination revealed flaccidity of the left leg, with partial paralysis; diminished muscular strength in the right leg; hyperactive tendon reflexes in the arms; areflexia in the legs, with a Babinski sign present bilaterally, and a sensory level at the

fourth thoracic segment. The cranial nerves were intact except for the optic nerves. The remainder of the general physical examination was not significant.

*Ophthalmologic Examination.*—The left eye was normal. Ophthalmoscopic study of the right eye revealed primary optic nerve atrophy. The pupils were equal and symmetric, and the reactions to light and in accommodation were present but sluggish. The motility of the eyes was normal. Vision was not determined.

*Laboratory Findings.*—The blood count was normal. Urinalysis showed a moderate number of white cells and a trace of albumin. Examination of the spinal fluid disclosed 86 cells per cubic millimeter, with 99 per cent lymphocytes and 1 per cent polymorphonuclear leukocytes; 240 mg. of protein, 40 mg. of sugar and 701 mg. of chlorides, per hundred cubic centimeters; a normal colloidal gold curve; a negative Wassermann reaction, and sterile cultures. All other laboratory findings were normal.

*Course.*—During hospitalization the patient had a low grade fever, with temperature usually under 101 F. As motor and sensory symptoms steadily progressed in severity, they also ascended to higher levels, so that on November 4 she began to experience respiratory difficulty. This increased so rapidly that, in spite of sedation and the use of the respirator, she died on November 7, forty-six days after the onset of the acute exacerbation of her illness.

*Clinical Diagnosis.*—The diagnosis was acute ascending myelitis.

*Autopsy.*—*Macroscopic Observations:* External examination revealed severe wasting of the muscles of the extremities. Internally, the heart and the abdominal viscera appeared normal; the lungs showed evidence of lobular pneumonia. The brain and the brain stem appeared normal. The optic nerves and the optic chiasm were flattened, and the right nerve was approximately one half as large as the left. The spinal cord appeared injured in the cervical segments on the left side, and white material oozed from the cut section. The cervical enlargement was swollen, soft and irregular; this swelling extended down to the fifth thoracic level. On section the cord showed pronounced edema of the parenchyma and obscuration of the architectural markings. The central gray matter had an abnormal granular appearance. Little bands of yellowish white material were scattered throughout the section, and in some places the cord was very soft, almost fluid.

*Microscopic Observations:* Histologically, the sections of the heart, aorta and most of the abdominal viscera were normal. The sections of lung showed active bronchopneumonia, and the sections of liver exhibited advanced atrophy of the parenchyma.

*Brain and brain stem.* There were no lesions of consequence at this level except for one small perivascular focus of demyelination in the subcortical white matter and occasional perivascular lymphocytic infiltration and edema in the lower portion of the medulla.

*Spinal cord.* In the cervical sections a large portion of all the white columns were involved in the pathologic process; the anterior and posterior gray horns had also been attacked. In the upper thoracic segments there was a large central area of demyelination, which included most of the gray substance and surrounding white columns; the involved area appeared microcystic. The lower thoracic sections showed widespread extensive demyelination of almost all the white and gray substance. The lumbar sections showed scattered foci throughout.

Histologically, these lesions of the cord were rarefied, microcystic and loose meshed and had lost their normal architectural markings. The process was one of acute necrosis, with destruction of all the neural elements. There were proliferation of microglia and conversion of microglia into phagocytes. There were

hyperplasia of astrocytes in some areas and degeneration of the same cells in others. Where the process had invaded the gray matter, there were destruction of the large nerve cells and the same proliferation of microglia. The perivascular spaces were packed with lipid-laden phagocytes. There were rarefied areas containing no cellular structure at all; these appeared to represent old, quiescent foci. The Mahon stain revealed extensive demyelination of all involved areas, although the demyelinated foci varied somewhat in size and in extent of demyelination. About the periphery of some of the lesions, numbers of huge, swollen myelin sheaths were seen undergoing fragmentation. With the Bodian stain, a great loss of axis-cylinders was demonstrated; some of the remaining axons were swollen, distorted and degenerated.

Optic nerves. There was a large area of demyelination in the right optic nerve which involved almost two thirds of the cross section. There were no swollen sheaths or axons in this lesion; apparently, the focus was not active. (These observations corroborated the clinical history.) There was some lymphocytic infiltration of the nerve sheath. With hematoxylin and eosin stain, a mild astrocytosis was seen in the substance of the nerve. The Bodian stain revealed a considerable loss of axis-cylinders in the large lesion. The left optic nerve and the optic chiasm showed no pathologic change in the sections available.

*Anatomic Diagnosis.*—The diagnosis was optic neuromyelitis.

*Summary.*—For two years this woman suffered from a subacute relapsing illness in which her eyes and spinal cord were the focal points attacked. Her first symptom was loss of vision in the right eye. A year later she had pain in the back and abdomen and constipation; an exploratory laparotomy was performed. After the operation, she immediately exhibited signs of paraplegia, and the diagnosis of poliomyelitis was advanced. She improved after six months of hospitalization and was allowed to go home. Three months later the progressive ascending paralysis returned and caused her death in six weeks.

Autopsy revealed a severe demyelinating and necrotizing process of the major portion of the spinal cord, the right optic nerve and the lower portion of the medulla. Microscopically, the important changes were demyelination of nerve fibers, destruction of axons, proliferation of neuroglia and perivascular infiltration. The process was oldest in the lumbar region of the cord and in the right optic nerve. A single microscopic lesion was discovered in the brain. The unique feature in this case was the comparatively long survival time (over two years).

CASE 5.—Mrs. B. S., a 46 year old Negro woman, was admitted to the Neurological Institute on May 2, 1947, with the history of increasing motor and sensory disability of the arms and legs for two months. Two months before admission the patient experienced sudden pain in the right flank, which descended during the first week as far as the right knee but did not progress farther. One month later she noted similar pain in the left side and leg; this was accompanied with pain in the right shoulder, radiating down the arm to the elbow. During this time the patient also noticed gradually progressive numbness down the right leg. She began to have difficulty in walking, which was also progressive. Four days prior to her admission there was a sudden increase in the paresis of the right leg; the

leg became so stiff that she could not move it, and she lost all sense of control over it. At this time she also noted weakness of the right arm and hand.

*Past History.*—The patient had had malaria as a child. Since her marriage she had borne six living children, and four induced abortions were performed, for economic reasons, between 1926 and 1931. She was admitted to the Presbyterian Hospital in 1931 for weakness and easy fatigability, of four months' duration. Physical examination revealed poor teeth, palpable liver and a spleen enlarged 3 fingerbreadths below the left costal margin. Laboratory examination disclosed severe anemia (hemoglobin, 35 per cent; red cells, 2,080,000) and a differential smear compatible with secondary anemia. The absence of free hydrochloric acid in the gastric contents was discovered, and she was given liver extract, without a reticulocyte response. She was then given a preparation of iron, and her red cell count rose to 3,950,000, with 54 per cent hemoglobin. The diagnosis of secondary anemia following repeated pregnancies and abortions was made, and she was discharged to the outpatient clinic, after having been given contraceptive advice. A moderate anemia persisted, and she continued to complain of weakness and lassitude. Liver extract and iron were prescribed regularly for several years.

The patient was again admitted to the Presbyterian Hospital in 1937, with acute otitis media. A myringotomy was performed, and she was kept for further studies of her anemia. In spite of the most thorough laboratory and clinical studies, no cause for the anemia was found. In 1942 she was placed under thyroid medication for the second time, but she remained weak and anemic. In 1944 the patient was readmitted to the Presbyterian Hospital for weakness and anemia. After a week of intensive liver therapy, without appreciable effect, she was given two transfusions of whole blood, which brought her red cell blood count up to 3,000,000. Because the patient presented such a serious diagnostic problem and because all other means of therapy had failed, splenectomy was performed, without benefit.

The patient was seen in the eye department of the Vanderbilt Clinic in July 1946, with a complaint of blurred vision in the right eye. Vision was 20/50 in the right eye and 20/20 in the left eye. With correction of + 1.00 D. sphere, vision in the right eye was 20/20. Examination of the eyes revealed nothing pathologic. Peripheral and central fields were within normal limits. Reexamination of the eyes in February 1947 revealed no abnormality.

*Examination.*—The patient was thin and underweight and appeared chronically ill; she was dull, uncooperative and mentally underproductive. She showed generalized lymphadenopathy, with pronounced enlargement of the axillary nodes. The spleen had been removed; the liver was palpable 2 fingerbreaths below the costal margin and was tender. The heart evidenced mitral and systolic murmurs (probably hemic). Neurologic examination revealed spastic paralysis of the legs and weakness of the right arm. The deep reflexes were exaggerated. Sensation was impaired in all extremities. The cranial nerves were intact except for the second; the fundi showed anemic changes, with pathologic pallor of the right optic disk. Vision was not determined. The ophthalmologic consultant found pallor of both optic disks, more advanced on the right than on the left. The remainder of the physical findings were apparently normal, but cooperation was so poor that this is not certain.

*Laboratory Findings.*—The average blood picture, determined on many occasions, was as follows: red cells, 2,620,000; hemoglobin content, 9.3 Gm. per hundred cubic centimeters; anisocytosis, poikilocytosis, macrocytosis and occasional nucleated red cells; white cells, 5,450, with a normal differential count. Persistent reticulocytosis, with a count of 6 to 10 per cent, was found, with a rise to 53 per cent

on treatment with folic acid (pteroylglutamic acid). The urine was always normal. Serologic reactions were normal. Examination of the cerebrospinal fluid revealed clear fluid, with normal dynamics; 10 cells per cubic millimeter, all lymphocytes; 140 mg. of protein per hundred cubic centimeters, a negative Wassermann reaction, and a colloidal gold curve of 2223322100. An abundance of additional laboratory data were compiled but failed to reveal the etiologic basis of her illness.

*Course.*—With minor remissions, the patient became progressively worse and presented the clinical aspects of fairly rapid ascending myelitis. On one occasion she again complained of severe abdominal pain, for which no cause was found. Liver and folic acid therapy, combined with several blood transfusions, failed to ameliorate her condition or check her downhill course, or appreciably to alter the blood picture. The spinal cord level was determined to lie at the fourth cervical segment shortly before her death, on Sept. 1, 1947.

*Clinical Diagnoses.*—The clinical diagnoses were (1) chronic anemia; type undetermined, and (2) ascending myelitis, cause undetermined.

*Autopsy.*—Macroscopic Observations: External examination was noninformative. Internal examination revealed that the spleen was absent and the liver very large. Clear amber fluid and many dense adhesions were found in the pleural cavities. The lungs presented a salmon gray appearance. The parenchyma of the brain had a marked pallor; the brain stem and cerebellum appeared normal. In the thoracic segments of the spinal cord, an irregularly outlined cavity was seen in the central portion of the cord. The cord at this level was flattened and reduced in consistency. On cut section, the normal architectural markings were obscured.

Microscopic Observations: The lungs presented the typical picture of bronchopneumonia. Since the changes in the liver, stomach, bone marrow and other organs were not clearcut and are not pertinent to this paper, only the pathologic changes in the central nervous system will be presented.

Brain and brain stem. Histologically, the cerebrum and brain stem, with the exception of the lower portion of the medulla, were normal. In the lower part of the medulla, lesions similar to those to be described in the spinal cord were scattered through the parenchyma; these lesions were smaller and less severe than those in the spinal cord.

Optic nerves. The hematoxylin and eosin stain revealed a large area of degeneration in the center of the right optic nerve; the connective tissue spaces between the nerve bundles appeared wider than normal and contained numerous perivascular collections of lymphocytes. There was considerable astrogliosis in the center of this lesion. The Mahon stains showed that this lesion conformed to a large, confluent area of demyelination, the center of which was more intensely demyelinated than the periphery (fig. 8). With the Bodian stain, a considerable loss of axons could be seen in the zone of demyelination. The left optic nerve appeared normal. The optic chiasm showed diffuse demyelination on one side, the right (fig. 9).

Spinal cord. The cervical segments of the cord presented many large and small areas of necrosis and demyelination in all the white columns (fig. 10 *a*). The thoracic sections showed such extensive necrosis and dissolution of tissue that they were unidentifiable. In the upper thoracic segments (fig. 10 *b* and *c*) there was an area of cavitation in the posterior white columns, in which all the neural elements had been destroyed. There were also diffuse rarefaction of most of one lateral white column and a zone of cystic degeneration near the periphery of the cord. In the middle thoracic segments (fig. 10 *d*) the area of cavitation



surrounded the central canal and extended dorsally through the posterior white columns and ventrally into both anterior gray horns. This degeneration in the anterior gray horns was associated with total disappearance of nerve cells and glial



Fig. 8 (case 5).—Mahon stain of the optic nerves. (A) The right optic nerve shows a large diffuse focus of demyelination in the center of the nerve. (B) The left nerve is normal and is included for comparison.

elements, leaving a loose-meshed microcystic tissue. On one side the cystic area extended ventrally through the anterior white columns to reach the pial surface.

Posteriorly, it likewise extended in bandlike fashion across the posterior white columns to reach the pial surface near one of the dorsal roots. In the lower thoracic segments (fig. 10 *e*) the cavitation was so extreme that the cord had lost its shape. Here, there was total destruction of most of the central gray matter. There were large, confluent areas of cavitation in the posterior white columns and macroscopically cystic lesions in the lateral white columns and, to a lesser degree, in the anterior white columns.

Histologically, the areas where neural elements could be recognized showed the same pathologic changes that have been described in the preceding 4 cases. The Mahon stain showed intense demyelination; the Bodian stain, a great loss of axons, and the phosphotungstic acid hematoxylin stain, considerable astrogliosis about the margins of the lesions. Perivascular lymphocytic infiltration and microglial proliferation with formation of phagocytes were seen throughout all the sections. In the most severely degenerated areas there was complete destruction of all the normal structures, leaving small cystic cavities which were bordered by partially degenerated tissue. In these zones the gray and white matter was rather loose and was composed of strands of glial tissue and persistent blood

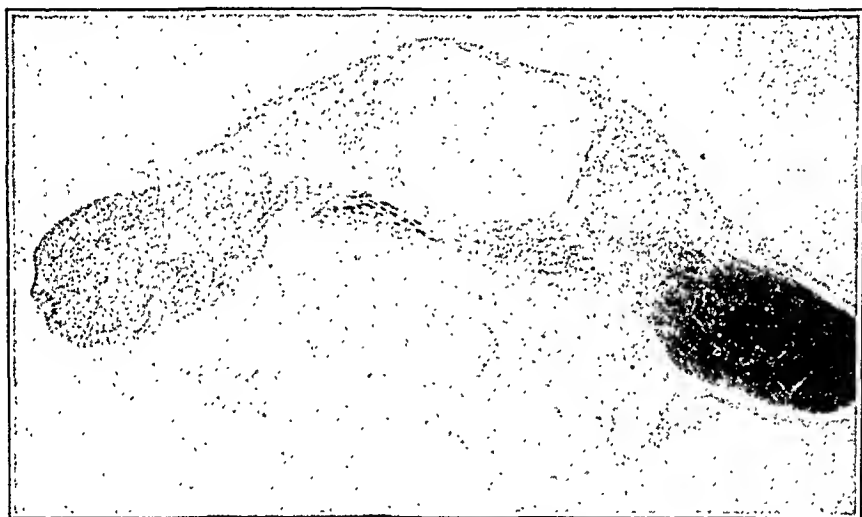


Fig. 9 (case 5).—Mahon stain of the optic chiasm, showing diffuse demyelination on one side (the right).

vessels. In the interstices of this spongy tissue were great numbers of coarsely vacuolated, lipid-laden phagocytes. There was no gliosis in any of the areas of necrosis.

The lumbar and sacral segments of the cord (fig. 10 *f*) were relatively normal.  
*Anatomic Diagnosis.*—The anatomic diagnosis was neuromyelitis optica.

*Summary.*—This case of long-standing anemia presented a difficult diagnostic problem. The following observations appeared significant: hepatosplenomegaly, hyperglobulinemia, anemia, leukopenia and gastric achlorhydria. Despite refractoriness to liver therapy for fifteen years, the patient did show a reticulocyte response to crude liver extract during her final hospitalization. An apparently unrelated neurologic syndrome appeared during the last four months of the patient's life; the signs and symptoms were those of an ascending myelitis, the nature of which was not determined clinically.

Necropsy revealed metaplasia of the gastric mucosa and hyperplasia of the bone marrow, such as is frequently seen in pernicious anemia. Although the early history does not fit into this classification, the terminal picture appears to do so. The patient, therefore, had two unrelated diseases.

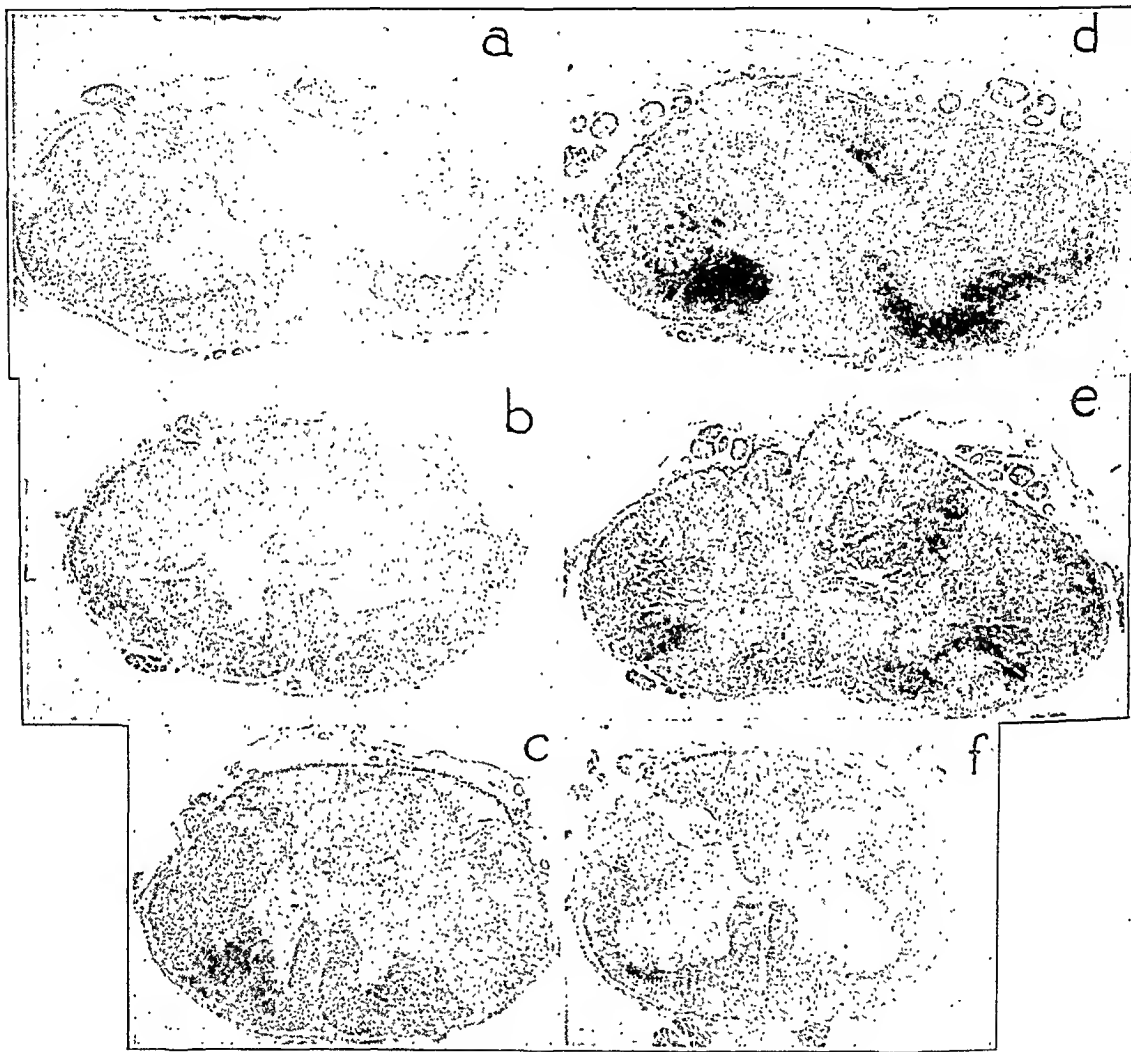


Fig. 10 (case 5).—Mahon stain of sections of the spinal cord, showing necrosis and gross cavitation of the thoracic segments: (*A*) cervical segment, (*B* and *C*) upper thoracic segments, (*D*) middle thoracic segment, (*E*) a lower thoracic segment and (*F*) a normal lumbar section.

In the central nervous system, autopsy disclosed necrotic lesions in the spinal cord and the right optic nerve; the spinal lesions were not confined to any tracts but were irregularly scattered throughout the substance of the cord. The presence of comparable changes in the spinal cord and the right optic nerve is consonant with the diagnosis of neuromyelitis optica.

## CLINICAL FEATURES

*Occurrence.*—Approximately 200 cases of neuromyelitis optica have been reported in the literature; the number is difficult to determine because of the numerous terms employed to designate this syndrome, and especially because of the doubts existing concerning its specificity. The disease occurs in both sexes; Michaux<sup>30</sup> found it commoner in females and Silbermann<sup>29</sup> in males. The syndrome probably occurs at any age; it has been reported in children of 9 years (Berliner,<sup>16</sup> Walsh<sup>17</sup>) and in a man of 60 years (Goulden<sup>10</sup>). Almost all the reported cases have occurred in white persons, but this may be due to the better medical care generally available to persons of the white race. It has recently been reported in Negroes (Dolgopol,<sup>22</sup> Silbermann<sup>29</sup>) and in a Chinese (Chang<sup>54</sup>); 2 of the cases in this report were of Negro women. There are no known occupational factors. Heredity apparently plays no part; there are no reports of its incidence in two generations of the same family.

*Onset.*—Prodromal symptoms are not unusual in cases of neuromyelitis optica. Mild antecedent illnesses, usually described as sore throat, "cold," "flu," headache, fever or simply malaise, are frequently noted in the published case reports. These symptoms usually precede the onset of the visual or spinal disability by a few days to two weeks.

In its most dramatic form, neuromyelitis optica occurs in a previously healthy young adult and is ushered in by sudden, complete loss of vision in one eye, followed by loss in the other eye a day or two later. An acute onset, whether the initial symptom is visual or spinal, is nearly always seen. With regard to the temporal priority of involvement of one system over the other, there is no accord. Katz<sup>11n</sup> discussed this first; of his 21 patients, 15 lost vision first, 1 showed spinal involvement first and 5 showed involvement of the two systems simultaneously. According to Goulden,<sup>10</sup> over 80 per cent of patients evidence loss of vision as the initial symptom; Henneberg,<sup>13d</sup> too, reported visual loss first in about 75 per cent of cases. Beck,<sup>12</sup> however, found the myelitis first in 52 per cent of cases, the blindness first in 25 per cent and the two together in 23 per cent of cases. Michaux<sup>30</sup> stated that it is of no importance which system is involved first. All have agreed that the time interval between involvement of the two systems is variable, from hours to days to weeks.

*Loss of Vision.*—In most of the reported cases the visual loss was rapid, severe and monocular; the visual acuity typically falls to light perception or complete amaurosis in one day. Recently, however, a number of cases have been reported with vision reduced only to 20/200; presumably, the patients had lost their central vision. The second eye is usually involved within a matter of days, and the loss is, again, as severe and rapid as in the first eye. The amaurosis is commonly

bilateral, although cases of monocular involvement have been reported (de Lapersonne,<sup>112</sup> Walsh<sup>17</sup> and cases 4 and 5 in this report). Walsh<sup>68</sup> described a few cases in which there was binocular loss of vision not followed by paraplegia; he declared that these cases represented an abortive form of neuromyelitis optica, explaining that the symptoms referable to the spinal cord may be minimal in some cases.

*Ocular Fundi.*—Considerable variation in the fundus picture early in this disease has been described, but only three types appear to occur commonly: (1) a normal fundus; (2) slight blurring of the margins of the disks with slight venous dilatation, and (3) acute papillitis, with edema of the disk, engorged veins, hemorrhages and exudates (Klar<sup>41</sup>). Later in the course of the process, optic nerve atrophy, of varying pattern, is found. Secondary optic nerve atrophy of the postpapilledema type is often described, or pallor of the disk may go on to primary optic nerve atrophy, with attenuation of the blood vessels. Michaux<sup>30</sup> divided his cases into two types according to the findings in the fundus: (1) retrobulbar neuritis, with a normal disk and a central scotoma (the patients with this type complain of pain, according to Michaux), and (2) papillitis, with varying degrees of severity. Michaux admitted that this division is not absolute; he stated that in many cases the process begins with the first type of optic disk and later shows frank papillitis. Goulden<sup>10</sup> stated that optic neuritis is almost always found and that retrobulbar neuritis is rare. Paton,<sup>69</sup> on the other hand, said that the characteristic lesion of neuromyelitis optica is a typical retrobulbar neuritis, with pain and loss of function. According to Paton, slight papilledema is sometimes seen but true papillitis is rare.

*Visual Fields.*—Many defects in the visual fields are possible and likely in neuromyelitis optica because of the irregular distribution of the lesions (Holden<sup>60</sup>) and because the chiasm is frequently involved. The commonest reported defect is a central scotoma, especially for colors (Fralik and DeJong,<sup>21</sup> and many others). The scotoma is usually bilateral, but monocular central defects are not rare. Hemianopsia was reported by Erb<sup>3</sup> and Holden<sup>60</sup>; the latter author stated that monocular hemianopsia is an important diagnostic aid in this syndrome.

58. Walsh, F. B.: *Clinical Neuro-Ophthalmology*, Baltimore, The Williams & Wilkins Company, 1947, pp. 783-790.

59. Paton, L.: Papilledema and Optic Neuritis: A Retrospect, *Arch. Ophth.* **15**:1-20 (Jan.) 1936.

60. Holden, W.: A Report of Four Cases of Acute Disseminated Myelitis with Retrobulbar Degeneration of Optic Nerves, *Arch. Ophth.* **40**:569-576, 1911; A Fifth Case of Acute Disseminated Myelitis with Retrobulbar Inflammation of the Optic Nerves, *ibid.* **43**:231-233, 1914.

Klar<sup>41</sup> found hemianopsia for colors, and he also described peculiar quadrantic defects with crescentic extensions. Halmajoz<sup>61</sup> reported a case with bitemporal hemianopsia. Concentric contraction of the peripheral fields has been reported in a number of cases, although the peripheral loss was not so severe and permanent as the central defect. Walsh<sup>58</sup> stated that the peripheral field becomes active before the central region in the patients who recover, and Chang<sup>54</sup> reported a case in which the central scotoma remained after the peripheral field had widened. In many cases of this disease the vision was so reduced that testing the fields was impractical and, further, many patients were too ill for testing. Thus, often the changes in field are not known.

*Palsies of Extraocular Muscles.*—Involvement of the extraocular muscles in neuromyelitis optica is uncommon but has been reported a few times. Michaux<sup>30</sup> found paresis of the right internal rectus muscle in his case. Walsh<sup>58</sup> reported 2 cases with muscular palsies: one with transient ptosis, and the other with a paretic squint that later became concomitant. McKee and McNaughton<sup>23</sup> described paralysis of conjugate movements of the eyes in their case. Complete ophthalmoplegias were reported by Bielschowsky,<sup>62</sup> Mahokian,<sup>11k</sup> Henneberg,<sup>13d</sup> Kerschensteiner<sup>11x</sup> and Perritt.<sup>63</sup> In case 3 of the present report there developed successively paralysis of convergence, paralysis of upward gaze and, finally, bilateral complete ophthalmoplegia.

*Pupils.*—The pupillary reactions in this disease are not characteristic; the dilatation of the pupil usually corresponds to the visual loss in the eye. In the acute stage of blindness, the pupils are widely dilated and react sluggishly, or not at all, to light. The pupillary reflexes return to the same degree as vision.

*Nystagmus.*—Nystagmus, so common in multiple sclerosis, is an exceptional symptom in neuromyelitis optica. When it occurs, it is assumed to have an amblyopic basis. Some authors have claimed that nystagmus has been reported only in cases in which the diagnosis was questionable. Putnam and Forster<sup>27</sup> described nystagmus in a case, but the diagnosis was later changed to multiple sclerosis. Michaux<sup>30</sup> employed the presence or absence of nystagmus as an important factor in differentiating neuromyelitis optica from multiple sclerosis.

*Pain.*—Pain in or about the eye is recorded in a minority of case reports. Bouchut and Dechaume<sup>13j</sup> reported pain in the orbits early in

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61. Halmajoz: Le syndrome de Devic au début d'une sclérose en plaques, *Rev. neurol.* **60**:178-178, 1933.

62. Bielschowsky, A.: *Myelitis und Sehnervenentzündung*, Berlin, S. Karger, 1901.

63. Perritt, R. A.: Optic Neuromyelitis, Report of Two Cases, *Arch. Ophth.* **11**:492-497 (March) 1934.

the course of illness in their case. The typical pain of retrobulbar neuritis was prominent in the case reported by Fralik and DeJong.<sup>21</sup> Retrobulbar pain, associated with blurring of vision, was the earliest sign of the disease in case 2 of the present report.

Pain associated with the myelitis is a commoner symptom. It was prominent in the symptoms of cases 4 and 5 of this report. McAlpine<sup>25</sup> stated that pain is a common early symptom of the disease, usually referable to the back, shoulder girdles or legs.

*Fever.*—Low grade fever has been reported in a few cases of neuromyelitis optica. The increase in temperature is indicative of poor prognosis, according to Michaux,<sup>30</sup> who stated that most patients with fever die.

*Cerebral Signs.*—All the symptoms of neuromyelitis optica are not referable to the optic nerves and spinal cord. General and local cerebral signs are not unusual. Devic<sup>7</sup> himself first called attention to the cerebral symptoms, and their occurrence has recently been emphasized by Wilson.<sup>64</sup> Among the cerebral symptoms that have been described are jacksonian epilepsy (Jumentié and Valière-Vialeix<sup>135</sup>); mental confusion (Genet and Devic<sup>131</sup>); headache, vomiting and dysarthria (Cestán, Riser and Planques<sup>36</sup>), and aphasia (Marinesco and associates<sup>32</sup>). Clouding of consciousness, delirium, fainting attacks, ataxia and tremors have also been described in this disease. Paroxysmal facial neuralgia characterized 1 of the cases reported by Collins.<sup>65</sup> In case 3 of the present report the patient exhibited euphoria, confusion, somnolence, disorientation as to time and place, poor coordination, dysarthria and coma. Because of the frequency of cerebral signs, Barrera<sup>66</sup> suggested "ophthalmoencephalo-myelopathy" as a more appropriate name for the disease.

*Paraplegia.*—The paraplegia of neuromyelitis optica is not distinctive; the most frequently reported type is a steadily progressive ascending myelitis, with both motor and sensory loss. Landry's paralysis has been suggested as the correct diagnosis, but the sensory loss rules against this syndrome. The neurologic signs may be indicative of any of the various forms of myelitis: (1) diffuse myelitis, involving several segments of the cord; (2) complete transverse lesion, at any single level; (3) Brown-Séquard syndrome, or (4) one or more small discrete lesions, involving one or several tracts. Considering

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64. Wilson, S. A. K.: *Neurology*, Baltimore, Williams & Wilkins Company, 1940, vol. 1, pp. 207-209.

65. Collins, J.: *Acute Myelitis and Thrombotic Softening of the Spinal Cord*, *Rev. Neurol. & Psychiat.* 10:157-173, 1912.

66. Barrera, S. E.: *Ophthalmo-Encephalo-Myelopathy: Clinico-Pathological Study of a Case*, *Psychiat. Quart.* 6:421-437, 1932.

the anatomic possibilities, one can readily comprehend the variability of the symptoms of the spinal cord, when both objective and subjective signs depend on the anatomic site of the lesion. Clinically, many combinations of upper and lower motor neuron lesions are seen; the deep reflexes may be lost, retained, increased or depressed. The paraplegia may be spastic or flaccid; it may change from one type to the other, or it may be spastic on one side of the body and flaccid on the other. Associated with the paralyses are all the known forms of sensory disturbance; particularly common are paresthesias, sensory loss in one leg, patchy sensory defects over the torso and extremities and a transverse sensory level in the thoracic region with complete loss below and a band of hyperesthesia above. Urinary and fecal retention or incontinence, giving rise to serious nursing problems, are seen in almost every case. The ascending paralysis eventually reaches the vital bulbar centers, and the common cause of death is respiratory paralysis. In the past, urinary infection and decubitus ulcer were prominent causes of death.

*Cerebrospinal Fluid.*—There has been no uniformity of opinion in regard to the spinal fluid findings. Most writers agree that the fluid is clear and that the pressure is not increased. Michaux,<sup>30</sup> however, stated that a slight increase in pressure was characteristic; he also expressed the opinion that increased albumin, moderate lymphocytosis and a noninformative colloidal gold curve were characteristic of Devic's syndrome. Mild pleocytosis has been reported in the majority of cases in which the spinal fluid has been examined; Popow's case<sup>43</sup> was unusual in that 3,000 cells per cubic millimeter were found. An increase in polymorphonuclear leukocytes in the spinal fluid was recorded by Fralik and DeJong,<sup>21</sup> Balser<sup>18</sup> and McAlpine.<sup>25</sup> An increase in protein, namely, the globulin fraction, has been reported by nearly every one who has examined the fluid. No abnormality has been found in the sugar of the spinal fluid, nor is the Wassermann reaction considered relevant. Colloidal gold curves are usually described as noncontributory.

*Course.*—Neuromyelitis optica may take one of three courses: (1) regression, to complete or nearly complete recovery; (2) one or more remissions, with an eventual fatal termination, or (3) a progressive downhill course to death. In those cases in which recovery occurs, visual acuity is usually regained before the functions of the spinal cord (McKee and McNaughton<sup>23</sup>). Vision may begin to improve within a week or two after the onset of the disease, and within a few weeks it may be normal. Walsh<sup>58</sup> stated that there is recovery of vision in the majority of cases and that he has seen only 1 case of permanent blindness. The paraplegia regresses more slowly, requiring several months before locomotion and sphincter control are regained



(Erb,<sup>3</sup> Seguin<sup>4</sup>). In many cases of recovery there are residual neurologic symptoms.

Beck<sup>12</sup> first drew attention to the occurrence of remissions in the course of neuromyelitis optica; he reported three complete remissions in his case and called them the first to be reported. In many cases improvement has been transient for a few days, but this is not considered a remission. Perritt<sup>63</sup> found that almost 50 per cent of the recorded cases have been characterized by remissions, a surprisingly high percentage in comparison with the estimates of others. In many of the cases with remissions the disease has eventually proved to be multiple sclerosis. In none of the more authentic cases with remissions has the patient lived.

In the third, and largest, group of cases, with the course progressing to death in the initial attack, a number of patients have died in a remarkably short time: Chisholm's<sup>5</sup> patient died in twelve days; Goulden's<sup>10</sup> in sixteen days; Dollfuss',<sup>31f</sup> in six days, and Uréchia and Veluda's,<sup>37</sup> in five days. Death early in the disease is usually attributed to encroachment of the ascending myelitis on the vital centers in the medulla, with ensuing respiratory paralysis. McAlpine,<sup>25</sup> however, stated that death more frequently results from paralysis of the phrenic nerves by a cervical lesion. Death also occurs later in the initial attack, sometimes after several months; in addition to respiratory failure, it may then be due to secondary complications, such as decubitus ulcer, ascending urinary infection or pulmonary infection. A few patients live for a considerable length of time; Dolgopol's<sup>22</sup> patient lived for three years and eight months.

*Prognosis.*—It has generally been accepted that the mortality rate of neuromyelitis optica is high, and most authors quote 50 per cent as the expected death rate. Devic<sup>7</sup> reported 5 deaths in his series of 17 cases. In each of Goulden's<sup>10</sup> series of 52 cases, 25 deaths, and in Beck's<sup>12</sup> series of 70 cases, 25 deaths were reported. Putnam and Forster<sup>27</sup> stated that the urinary infection, decubitus and respiratory failure may be prevented by mechanical means, that the present mortality rate is extremely low and that the outlook for improvement is fairly good. On the other hand, Hassin<sup>20</sup> stated that the pathologic process of this disease is so severe that recovery cannot be expected. It is difficult to form an accurate estimate of the mortality rate in this syndrome because the diagnosis is obviously uncertain in the cases of recovery.

*Treatment.*—When the etiology and pathogenesis of a disease are unknown, therapy is usually unsatisfactory, and this is certainly true of neuromyelitis optica. In the early cases all manner of medicines were used, none of which proved efficacious. Arsenic, commonly employed abroad for multiple sclerosis, is contraindicated in cases of

neuromyelitis optica, according to Brain.<sup>67</sup> A cure in 1 instance (Haynes<sup>68</sup>) was attributed to vitamin B therapy. Putnam and Forster,<sup>27</sup> who stated the belief that most patients can be saved, recommended good nursing care, tidal drainage for the cystitis and use of the respirator for the respiratory paralysis. In view of the new allergic theory of the causation, Silbermann<sup>29</sup> suggested that desensitization with histamine or allied substances may prove helpful. Surgical intervention, i. e., exploratory craniotomy, ventriculography, and even lumbar puncture, is not contraindicated in this condition, according to Walsh,<sup>58</sup> Woods<sup>69</sup> and Schaltenbrand,<sup>70</sup> all of whom have reported death soon after such measures were attempted. The only measures that can be recommended at present are good nursing care and proper hygienic attention to the skin, urinary and intestinal tracts and musculature; tidal drainage will eliminate, or at least reduce, deaths from urinary sepsis. There is no known specific therapy.

*Summary of Clinical Features.*—It is obvious from the preceding paragraphs that the literature abounds in contradictions concerning the clinical findings in neuromyelitis optica. For example, Goulden found loss of vision the initial symptom in over 80 per cent of cases, while Beck, surveying much the same group of cases, found visual loss first in only 25 per cent of cases. Likewise, Goulden stated that optic neuritis is commonly found and that retrobulbar neuritis is rare, while Paton claimed that retrobulbar neuritis was the characteristic lesion and that papillitis was rare. Therefore, in an endeavor to determine more accurately the clinical features of neuromyelitis optica, 15 of the most complete case reports published in the last twenty years were studied, mainly from an ophthalmologic point of view, and the data combined with those of the 5 cases presented in this report. Only cases in which the diagnosis was substantiated by autopsy have been selected; thus, whether or not neuromyelitis optica is a specific entity, these cases are proved examples of what is customarily considered neuromyelitis optica. The data are presented in table 1. When there was any question of interpretation (as in the visual acuity in a number of cases) the findings are given in the words of the author and are in parentheses.

The following conclusions may be drawn from these 20 case reports:

Age: Neuromyelitis optica may occur at any age but is commoner in persons between 30 and 50 years of age.

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67. Brain, W. R.: Diseases of the Nervous System, London, Oxford University Press, 1947, pp. 486-516.

68. Haynes, G. W.: Neuromyelitis Optica: Report of a Case, Arch. Neurol. & Psychiat. **43**:1267-1269 (June) 1940.

69. Woods, A. G., in discussion on McKee and McNaughton,<sup>23</sup> pp. 136-137.

70. Schaltenbrand, G.: Hirngeschwulstähnliche Erkrankungen die reine Geschwülste sind, Ztschr. f. d. ges. Neurol. u. Psychiat. **161**:162-166, 1938.

TABLE 1.—Clinical Picture of

Case No.	Author	Age	Sex	Initial Symptom	Visual Loss	Field Defect	Fundus Findings	Remissions
1	Beek <sup>12</sup> .....	15	F	Visual	"Nearly blind, both eyes"	Bitemporal hemianopsia early; later, large central scotomas, both eyes	Secondary optic atrophy early; primary optic atrophy later	3
2	Walsh.....	9	F	Visual	Light perception, both eyes	No report	Pallor of disks and blurring of disk margins of both eyes	0
3	Fralik and DeJong <sup>21</sup>	31	M	Visual	Hand movements, both eyes	Large, central scotoma, both eyes	Marked optic neuritis early (both eyes); secondary optic atrophy (both eyes) later	1
4	Balser <sup>18</sup> (case 1)	42	F	Spinal	"Completely blind"	No report	Blurring of disk margins and hyperemia	0
5	Balser <sup>18</sup> (case 2)	50	F	Spinal	20/60, both eyes	Full to confrontation test, early	Blurring of disk margins	0
6	Balser <sup>18</sup> (case 3)	15	F	Spinal	Blind, left eye; later: 20/60 right eye; 20/80 left eye	Constriction of peripheral fields (both eyes), with a pericentral scotoma (left eye)	Pallor of disk of left eye	2
7	Dolgopoi <sup>22</sup>	35	F Negro	Spinal	"Poor, with progressive impairment"	Normal (early)	Pallor of disks, greater in left eye	1
8	Cone, Russel and Harwood <sup>16</sup>	36	M Negro	Visual	"Complete blindness"	Large central scotoma (both eyes); normal peripheral fields	Pallor of disks, more in right eye; later marked optic atrophy (both eyes)	1
9	Noran and Polan	48	F	Visual	"Total blindness, both eyes"	No report	"Optic nerve atrophy"	2
10	Kohut and Richter <sup>28</sup>	43	F	Spinal	Right eye: no light perception; left eye: approximately normal	No field in right eye; field of left eye full to confrontation test	Right eye: acute optic neuritis, with edema, hemorrhages and exudate; left eye: slight blurring of disk margins	None
11	Hassin <sup>20</sup> ....	33	F	Spinal	Right eye: hand movements; left eye: no light perception	No report	Right eye: mild pallor of the disk; left eye: slight blurring of the disk	1
12	Hurst, de Crespigny and Fry	46	F	Visual	Right eye: no light perception; left eye: no light perception	No report	White disks, showing optic atrophy and small vessels (both eyes)	4
13	McAlpine <sup>14</sup> (case 1)	24	F	Spinal	Both eyes: light perception, early; later, "blind, both eyes"	No report	"Optic atrophy, both eyes"	1
14	McAlpine <sup>14</sup> (case 2)	26	F	Spinal	Right eye: light perception; left eye: counting fingers	Large, central scotoma (left eye)	Blurred disk with full veins, right eye, and temporal pallor of disk, left eye; later, optic atrophy (both eyes)	2
15	Lowenberg, DeJong, and Foster	45	M Physician	Visual	No report	No report	Moderate optic atrophy (both eyes)	1
16	Stansbury, (case 1)	31	F Negro	Visual	Right eye: 20/20; left eye, 20/200	Large, central scotoma (left eye)	Right eye: normal; left eye: moderate temporal pallor	None
17	Stansbury, (case 2)	57	M	Visual	Right eye: 20/200; left eye, 20/200	Large, central scotoma (both eyes)	Blurring of disks (both eyes)	None
18	Stansbury, (case 3)	18	F	Spinal	"Poor vision, both eyes"	Patient too ill for field testing	Pallor of disks (both eyes)	None
19	Stansbury, (case 4)	29	F	Visual	"Blind, right eye"	No examination	Primary optic atrophy (right eye); normal (left eye)	2
20	Stansbury, (case 5)	46	F Negro	Spinal	Right eye: 20/50; left eye: 20/20 (early)	Fields normal (early)	Pallor of optic disk (right eye); normal (left eye)	None

Length of Disease	Spinal Fluid	Course of Paraplegia
13 mo.	4 cells/cu. mm.; protein 0.04 mg./100 cc.; weak syphilitic curve in Lange test	Back pain; weakness and numbness of legs; paralysis of legs; incontinence of urine and feces; improvement; recurrence of previous symptoms; paresthesias; complete paralysis of arms and legs; sensory loss to sixth thoracic level; hyperactive reflexes; respiratory failure; death
6 wk.	Normal pressure and dynamics; 27 cells/cu. mm. (80% polymorphonuclear cells, 20% lymphocytes); sterile culture; nonprotein nitrogen 20 mg., chlorides 712 mg. and sugar, 58 mg./150 cc.	Tingling and weakness of feet; flaccid paralysis of legs; loss of sphincter control; patchy sensory loss; variable reflexes; weakness of arms; loss of sensation below nipple line; dermatographia; hypesthesia of face; apathy and drowsiness; flaccid paralysis of arms; diaphragmatic respiration; dysarthria; dysphagia; death
2 mo.	Pressure 230 mm. water; 10 lymphocytes/cu. mm.; globulin 4+; colloidal gold curve 0001110000	Numbness of feet; staggering; weakness and numbness of legs; hyperactive reflexes; constipation; inability to walk; urinary incontinence and fecal retention; sensory loss below seventh thoracic level; urinary infection; decubitus ulcers; respiratory failure; death
9 wk.	184 cells/cu. mm. (15% polymorphonuclear cells); protein content, Wassermann reaction and gold curve normal	Asthenia and pains in legs; pain in shoulders and neck; rigidity of neck; incontinence of urine and feces; sensory loss to sixth thoracic level; abnormal reflexes; respiratory difficulty; death
7 wk.	38 cells/cu. mm.; protein 110 mg./100 cc.; Wassermann reaction negative; colloidal gold curve normal	Numbness of feet; weakness of legs; numbness and weakness of left arm; incontinence of urine and feces; poor coordination; progressive sensory loss; abnormal reflexes; death from respiratory paralysis
20 mo.	15 cells/cu. mm.; protein 40 mg./100 cc.; Wassermann reaction negative; colloidal gold curve normal	Numbness and paresis of right leg and then of the left leg; weakness of left hand; loss of deep reflexes; loss of sensation below umbilicus; gradual deterioration to death
44 mo.	20 cells/cu. mm.; slight increase in globulin; sugar normal; Wassermann reaction negative; colloidal gold curve 0112332100	Numbness of legs; unsteady gait; numbness and paralysis from waist down; incontinence of urine and feces; abnormal reflexes; sensory loss to tenth thoracic level; improvement; return of previous sight; spastic paraplegia; gradual deterioration; death from pneumonia
8 mo.	Pressure 170 mm. water; 7 cells/cu. mm.; globulin reaction negative; protein 113 mg./100 cc.; reaction for lead positive	Tingling, weakness and numbness of legs; urinary retention and constipation; patchy hypesthesias and hyperesthesias; inability to stand; loss of reflexes in legs; paralysis of legs; ascending sensory loss; death
20 mo.	Pressure 7-14 mm. Hg; 4 cells/cu. mm.; protein 45 mg./100 cc.; sugar 60 mg.; colloidal gold curve normal	Numbness of feet; sensory loss to fifth thoracic level; paralysis of legs; improvement; numbness of legs; complete motor and sensory paraplegia; bladder and rectal incontinence; areflexia in lower extremities; progressive motor and sensory loss; diaphragmatic breathing; death
6 wk.	Pressure 140 mm. water, normal dynamics; 185 cells/cu. mm.; 70% polymorphonuclear cells, 30% lymphocytes; protein 241 mg./100 cc.; Wassermann reaction negative; culture sterile	Numbness of thighs; burning sensations of feet and ankles; ascending numbness; weakness of knees; inability to stand; flaccid paralysis of legs with areflexia; sensory loss to waist; stiff, painful neck; sensory loss to nipple line; weakness of arms; loss of sensation in arms; diaphragmatic respiration; death
14 mo.	No report	Pains, weakness and numbness in right leg and then in the left leg; ascending numbness to breasts; paralysis of legs; improvement; paralysis of legs again; anesthesia to umbilicus; automatic bladder; paralysis of right arm, then of left arm; constipation; restlessness and disturbed sensorium; death
20 mo.	20 lymphocytes/cu. mm.; protein 70 mg./100 cc.; increased globulin; colloidal gold curve 1112221000; Wassermann reaction negative	Girdle pains; urinary retention; lumbar pain, spreading to buttocks, thighs and legs; loss of strength and sensation in legs; hyperreflexia, then areflexia; urinary incontinence; constant pain; sensory loss to nipple line; delirium; urinary sepsis; death
18 mo.	4 lymphocytes/cu. mm.; protein 0.03 mg./100 cc.; Wassermann reaction negative; colloidal gold curve 1111222100	Pain in shoulders; paresthesias and weakness of legs; urinary retention; paralysis of abdominal and intercostal muscles; paralysis of legs; variable reflexes; loss of sensation to fourth thoracic level; fecal incontinence; improvement; abdominal pain; paralysis of legs again; loss of sphincter control; paresthesias in arms and legs; paresis of hands and wrists; decubitus ulcers and cystitis; death
26 mo.	Pressure 130 mm. water; 2 cells/cu. mm.; protein 0.025 mg./100 cc.; colloidal gold curve normal	Pain in shoulders; numbness and weakness of legs and abdomen; urinary retention; sensory loss to sixth thoracic level; drowsiness; pain and paresis of arms; complete flaccid paralysis of legs and arms; diaphragmatic breathing; improvement; urinary infection and incontinence; improvement; pain in neck; incontinence; paresis and sensory loss again; vomiting; respiratory paralysis; death
14½ mo.	30 lymphocytes/cu. mm.; otherwise normal	Paresthesias of right arm, leg and abdomen; Horner's syndrome on right; spastic paralysis of right arm and leg; hyperreflexia; patchy anesthesia; hiccups; dysuria; improvement; paresthesias; paralysis of left arm and leg; respiratory difficulty; overflow incontinence; painful paresthesias; death from respiratory paralysis
3 mo.	Normal pressure and dynamics; 10 cells/cu. mm.; globulin 1+; protein 56 mg., sugar 62 mg. and chlorides 702 mg./100 cc.; Wassermann reaction negative; colloidal gold curve 1233332100	Numbness and weakness of right arm and leg; numbness of left leg and foot, then of left hand; hyporeflexia of arms and hyperreflexia of legs; hypesthesia of all extremities; urinary retention; excessive perspiration about head and neck; marked paralysis of all four limbs; respiratory paralysis; death
5 mo.	Normal pressure and dynamics; no cells; protein 60 mg., sugar 94 mg. and chlorides 681 mg./100 cc.; gold curve 1111100000; Wassermann reaction negative	Staggering; poor coordination; hyperreflexia; weakness of arms and legs; falling; tingling sensation in arms and legs; noise in ears; dizziness; ataxia; increasing weakness of extremities; reduced pharyngeal reflex; deviation of uvula; respiratory embarrassment; death
6 wk.	Normal pressure and dynamics; 9 cells/cu. mm.; protein 63 mg. and sugar 65 mg./100 cc.; gold curve 1100000000; Wassermann reaction negative; cultures sterile	Weakness and numbness of left arm and leg; unsteady gait; slurring of speech; euphoria and confusion; somnolence; weakness of right arm and leg; disorientation; loss of sensation on right; hyperreflexia; incontinence of urine and feces; bilateral third and sixth nerve palsies; left hemiplegia with spastic arm and flaccid leg; right hemiparesis; complete bilateral ophthalmoplegia; coma; decerebrate posture; respiratory embarrassment; death
2 yr.	Normal pressure and dynamics; 86 cells/cu. mm. (99% lymphocytes); protein 240 mg., sugar 40 mg. and chlorides 701 mg./100 cc.; Wassermann reaction negative and gold curve normal	Pain in back and abdomen; constipation; weakness of legs, with areflexia; improvement; paresthesias of abdomen and legs; sensory loss to breasts; urinary retention; constipation; pain in shoulders and neck; numbness and paresthesias in arms; areflexia in legs and hyperreflexia in arms; respiratory difficulty; death
6 mo.	Normal pressure and dynamics; 10 lymphocytes/cu. mm.; protein 140 mg./100 cc.; Wassermann reaction negative; cultures sterile; gold curve 2223322100	Pain in right flank; numbness and weakness of right leg, then of right arm and hand; pain in left leg and elbow; numbness of left leg; difficulty in walking; progressive paralysis of all four limbs; severe abdominal pain; vomiting and prostration; respiratory paralysis; death

Sex: The disease appears to be commoner in persons of the female sex; of these 20 patients, 16 were female.

Race: The disease is not limited to persons of the white race; 4 of the 20 patients were Negroes.

Initial Symptom: The incidence of the initial disability was distributed equally between the visual system and the spinal cord in this series of cases; in 50 per cent loss of vision, and in 50 per cent neurologic symptoms were first.

Loss of Vision: Severe binocular loss of vision is characteristic of this syndrome. The degree of visual loss varied in the 20 cases as follows:

Binocular loss	No. of Cases
Blind .....	5
"Nearly blind" .....	1
Light perception .....	3
Hand movements .....	1
20/200 .....	1
20/60 to 20/200.....	3
Monocular loss	
"Blind" .....	3
20/200 .....	1
20/50 .....	1
No record of the visual acuity.....	1

Ophthalmoscopic Appearance: Terminally, in the majority of cases of neuromyelitis optica, optic nerve atrophy is exhibited. Of the 16 cases of this series in which the diagnosis of optic nerve atrophy was made, primary or secondary optic atrophy was described in 5; of the remaining 11 cases, the diagnosis was simply "optic nerve atrophy" in 6 and "pallor of the disks" in 5. Of the 16 cases with optic nerve atrophy, the lesions were binocular in 12. The diagnosis in the remaining 4 cases would appear to be optic neuritis, which was binocular in 3 cases.

Unfortunately, the descriptions of the fundi were too inaccurate for careful ophthalmologic analysis. Most of the patients were not examined early in their illness, and none of the case reports contain detailed, repeated observations. In addition, most of the examinations were reported by neurologists who are not accustomed to classify optic nerve atrophy according to ophthalmologic usage.

Visual Fields: Either central scotoma or loss of the entire field appears to be the characteristic field change. Large central scotomas were demonstrated in 6 cases in this series, being binocular in 4 cases and monocular in 2. Five patients were blind, and so presumably had no field, and 1 patient was blind in one eye. General constriction of the peripheral fields with a pericentral scotoma in one eye was recorded in 1 case. The fields were reported to be normal in 1 case. There was no description of the field in 6 cases.

Remissions: Remissions occurred in about half of the cases in this series (12 cases, or 60 per cent). The distribution of remissions was as follows:

No. of Remissions	No. of Cases
1 .....	6
2 .....	4
3 .....	1
4 .....	1
None .....	8

Length of the Disease: According to the experience of these 20 patients, a person with neuromyelitis optica is likely to die in the first three months of his illness or at some time in the second year. Seven patients in this group died within three months, and 8 died in the second year of the process.

Paraplegia: The characteristic neurologic feature in this series of cases was the variability of the clinical picture. There appears to be no pathognomonic neurologic sign or symptom in this syndrome. The initial neurologic complaint was referable to the legs in 11 cases, and the initial symptom was sensory in 13 cases. Pain was a prominent feature in 10 of the cases. The deep reflexes were always variable. The paralyses were sometimes flaccid and sometimes spastic. Cerebral symptoms were noted in 7 cases. Incontinence of the bladder and rectum was specified in 15 case reports. Respiratory paralysis was the cause of death in 14 cases. Death was due to pneumonia in 1 case, and the cause of death was not clear in 5 cases. The only consistency in the neurologic symptomatology was the ascending nature of the process; in all 20 cases, including those in which the initial symptom was located elsewhere, the legs were involved early and the rest of the body in an irregular, but generally ascending, pattern.

Spinal Fluid: There is no change in the spinal fluid characteristic of neuromyelitis optica.

If these 20 cases are representative of neuromyelitis optica, one may conclude that this disease occurs more commonly in females in the first half of life and is ushered in by either optic or spinal disability. Ophthalmologically, binocular loss of vision, optic nerve atrophy and field changes are characteristic. Neurologically, variability is the rule in this rapidly ascending myelitis. No laboratory findings are peculiar to the disease. Remissions are seen in about half the cases. In the fatal cases death usually occurs within two years.

*(To Be Concluded)*

# News and Notes

EDITED BY DR. W. L. BENEDICT

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## GENERAL NEWS

**Graduate Training in Ophthalmology.**—The University of Toronto Faculty of Medicine is offering a postgraduate course in ophthalmology extending over three years. The first year, on a fellowship, the value of which is approximately \$1400, the student spends in one of the basic sciences of ophthalmology, and the second and third years are spent in the intern service of one or more of the university teaching hospitals. Approximately four hours a week of didactic teaching are arranged for the students by members of the staff. On Saturday mornings staff ward rounds are made at the Toronto General Hospital and are attended by the interns from the other teaching hospitals. A sound knowledge of neurology and metabolic diseases is desirable. The fee for instruction is \$50 a year, payable to the chief accountant, University of Toronto.

An application for appointment may be made to the Professor of Ophthalmology, University of Toronto Faculty of Medicine. Appointments are made in December, to commence July 1.

**Course in Histopathology of the Eye, New York Eye and Ear Infirmary.**—The schedule of the three months' course in histopathology of the eye at the New York Eye and Ear Infirmary, given by Dr. Brittain F. Payne and associates, has been rearranged to last one week from Jan. 9 to 14, 1950.

The course will be given in the afternoons and will consist of the same number of hours of instruction and of the same material as those previously allotted. Further information may be obtained by writing to the Post-Graduate Division of the New York University College of Medicine.

**Postgraduate Course in Ophthalmology, University of California Medical School.**—The University of California Medical School announces a postgraduate course in ophthalmology for qualified physicians, Sept. 12 to 17, 1949, to be given at the University of California Medical Center, San Francisco, under the sponsorship of the University Extension (Medical Extension), University of California. Complete program and further details may be obtained from Dr. Stacy R. Mettier, head of postgraduate instruction, Medical Extension, University of California Medical Center, San Francisco 22.

**Transactions of the American Ophthalmological Society.**—The *Transactions*, published in book form, may be purchased by advance subscription. The current volume contains theses of applicants for membership and the scientific papers given at the eighty-fifth annual meeting in June 1949. The price is \$12. Copies may be procured by order to the editor, Dr. Wilfred E. Fry, 1930 Chestnut Street, Philadelphia. Orders must be in by December 1.

## SOCIETY NEWS

**Joint Meeting of North Carolina Eye, Ear, Nose and Throat Society and South Carolina Society of Ophthalmology and Otolaryngology.**—A joint meeting of the two societies will be held at the Hotel Poinsett, Greenville, N. C., Sept. 12 to 15, 1949. The program follows:

Dr. A. D. Ruedemann, professor of ophthalmology, Wayne University, Detroit:  
Differential Diagnosis of Unilateral and Bilateral Ocular Protrusion  
End Results with New Radium D Applicator as Compared with Results with Radon  
Ocular Manifestations of Allergy

Dr. Peter C. Kronfeld, department of ophthalmology, Illinois Eye and Ear Infirmary, University of Illinois, Chicago:  
Differential Diagnosis of Acute Glaucomas  
Prognosis of Retinal Detachment  
Newer Drugs in Ophthalmology

Dr. Rudolph Aebli, professor of ophthalmology, New York University, New York:  
Relation of Muscle Imbalances to Palpebral Aperture and Pseudoptosis  
Principles of Ocular Muscle Surgery  
Congenital Muscle Anomalies

Dr. Carl C. Johnson, associate, department of ophthalmology, Harvard Medical School, Boston:  
Surgical Treatment of Ptosis  
Diagnosis and Surgical Treatment of Glaucoma

Dr. Preston C. Iverson, New York:  
Neoplasms of Lip, Nose and Eyelid and Plastic Repair of the Lesions  
Congenital Deformities of the Face

Dr. Louis H. Clerf, Philadelphia:  
Cough Viewed from the Otolaryngologic Standpoint  
Surgical Treatment of Paralysis of Larynx  
Malignant Neoplasms of Larynx

Dr. Kenneth M. Day, Pittsburgh:  
Clinical Management of Deafness  
Ménière's Disease

Dr. Russell A. Sage, Indianapolis:  
Diseases of the Mouth and Tongue

**Ophthalmological Society of Egypt to Award Prize.**—The Ophthalmological Society of Egypt, to encourage scientific work in ophthalmology, has decided to grant a prize, to the value of 20 Egyptian liras, for the most valuable contribution presented before the Annual Congress of the Society. The competition is open to all members of the Society of less than twenty years' practice. The subject is left open. Articles must be received in Cairo not later than the beginning of December. Further details may be secured from the honorary secretary, Ophthalmological Society of Egypt, Dar El Hekma, 42 Kasr El Ainy Street, Cairo, Egypt.



**Officers of New York Society of Clinical Ophthalmology for 1949-1950.**—The officers elected for the coming year are: president, Dr. Sidney A. Fox; vice president, Dr. Samuel Gartner; recording secretary, Dr. Bernard Kronenberg; corresponding secretary, Dr. Leon H. Ehrlich; treasurer, Dr. Edward Saskin; librarian, Dr. Howard Agatson.

The retiring president, Dr. Benjamin Esterman, was elected to the advisory council.

#### UNIVERSITY NEWS

**Appointments by the University of Toronto Faculty of Medicine.**—The University of Toronto Faculty of Medicine has appointed Dr. H. L. Ormsby as clinical teacher in charge of bacteriology of the eye, and Dr. O. B. Richardson, clinical teacher in charge of pathology of the eye, in the department of ophthalmology.

# Abstracts from Current Literature

EDITED BY DR. WILLIAM ZENTMAYER

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## Cornea and Sclera

CORNEAL TRANSPLANTATION, R. T. PATON, J. M. McLEAN, R. CASTROVIEJO, A. E. MAUMENEE and W. KORNBLUETH, *Am. J. Ophth.* 31:1365 (Nov.) 1948.

This is a symposium in which Paton discusses selection of cases; McLean, technics; Castroviejo, complications, and Maumenee and Kornbluth, physiopathology. The last is in the form of a statistical study.

W. S. REESE.

TREATMENT OF ROSACEA KERATITIS. J. JIRMAN, *Ann. d'ocul.* 181:475 (Aug.) 1948.

The author reviews the various ocular manifestations of keratitis rosacea and the etiologic factors suggested for this important disease of the eyes. A case of keratitis rosacea occurring in both eyes of a woman aged 54 is described in detail. She received a therapeutic trial of practically every means ever suggested for keratitis rosacea, i. e., autohemotherapy and use of riboflavin antihistamic drugs and hormones, without control of the corneal disease. Finally, one eye was covered with a conjunctival flap. There were immediate regression of symptoms and gradual objective improvement. The other eye showed no improvement until it was covered with a similar flap.

If the flap retracts within three to four days, little improvement is noted. The sutures holding the flap should be deep, so that the flap covers the cornea for ten to fifteen days. This permits the conjunctiva to take an active part in the healing of the cornea.

P. R. McDONALD.

## Glaucoma

PRESSOR TEST FOR GLAUCOMA. G. T. STINE, *Am. J. Ophth.* 31:1203 (Oct.) 1948.

Stine found the pressor test safe and easily performed for the detection of wide angle glaucoma but completely unreliable in the detection of narrow angle glaucoma.

W. S. REESE.

ELLIOT TREPHINING OPERATION FOR GLAUCOMA. R. E. MEEK, *Am. J. Ophth.* 31:1232 (Oct.) 1948.

Meek recommends use of Tenon's capsule as part of the bleb, and he modifies the operation by making an incision at the limbus so that corneal splitting is facilitated.

W. S. REESE.

ALLERGY IN GLAUCOMA. C. BERENS, L. J. GIRARD and E. CUMMINGS, *Ann. Allergy* 5: 526 (Nov.-Dec.) 1947.

Three cases of chronic simple glaucoma are presented in which the usual treatment with miotics and attempted desensitization with autogenous bacterial antigens had been supplemented by the removal from the diets of food allergens, as determined by the pulse-diet method. In 1 case, the hitherto uncontrolled tension was brought under control apparently only after the institution of an allergen-free diet. In the other 2 cases, surgical and medical treatment controlled the glaucomatous hypertension but failed to check progressive loss of visual fields. The fields showed striking improvement after the institution of an allergen-free diet. The authors conclude that, while the findings are suggestive, it is inadvisable to draw definite conclusions.

W. ZENTMAYER.

### Experimental Pathology

OBSERVATIONS ON EXPERIMENTAL PNEUMOCOCCAL INFECTION OF THE RABBIT'S CORNEA AND ON THEIR TREATMENT WITH PENICILLIN. J. MACASKILL and M. WEATHERALL, *Brit. J. Ophth.* 32: 892 (Dec.) 1948.

The article reports further observations on the lesions produced by intracorneal inoculation of the same and other strains of pneumococci and on the effect of penicillin administered subconjunctivally on these lesions in animal experimentation. The following summary is supplied: The responses of rabbits to intracorneal injections of various strains of pneumococci are described. The lesions were variable, but with one or two strains keratitis, iritis and hypopyon were produced with sufficient constancy to permit the evaluation of therapeutic procedures. Penicillin was found to be more effective when administered subconjunctivally than subcutaneously, and by the former route completely to arrest infection when 1,000 units per kilogram of body weight were given at twelve hour intervals.

W. ZENTMAYER.

### General

PSYCHOSOMATIC INTERRELATIONSHIPS IN OPHTHALMOLOGY. D. O. HARRINGTON, *Am. J. Ophth.* 31: 1241 (Oct.) 1948.

Harrington decries the lack of interest manifested by ophthalmologists in psychosomatic medicine and discusses five ocular conversion symptoms and an equal number of ocular vegetative neuroses.

W. S. REESE.

TREATMENT OF DELAYED POSTOPERATIVE FORMATION OF THE ANTERIOR CHAMBER. V. A. BYRNES, *Am. J. Ophth.* 31: 1261 (Oct.) 1948.

Byrnes believes that no anterior chamber should be allowed to remain flat more than five days after cataract extraction. For flat chambers he recommends inspection of the wound and cauterization of the wound with a heated squint hook or use of a diathermy needle, such as that employed in treatment of retinal detachments. He reports 5 cases.

W. S. REESE.

ON NEW TYPES OF OCULAR DISEASES. A. FUCHS, *Am. J. Ophth.* 31:1273 (Oct.) 1948.

Among new types of ocular disease Fuchs includes divided nevi, Sjögren's syndrome, Behcet's syndrome, keratitis parenchymatosa linearis, neuritis syphilitica papulosa, myopia inversa, choroiditis proliferans and neuritis retrobulbaris maligna.

W. S. REESE.

### Injuries

FRIEDLÄNDER'S BACILLUS INFECTION FOLLOWING PERFORATING WOUND OF ORBIT. W. J. CRAWFORD, *Am. J. Ophth.* 31:1293 over some of the test letters.

Crawford reports a case of infection of the orbit with Friedländer's bacillus following a perforating injury which improved after removal of a foreign body and treatment with streptomycin.

W. S. REESE.

TREATMENT OF SUPERFICIAL CORNEAL INJURIES. A. R. SHERMAN, *Am. J. Ophth.* 31:1467 (Nov.) 1948.

Sherman remarks the slowness of healing of certain superficial traumatic corneal lesions. For these he uses a binocular bandage to encourage epithelial regeneration. He briefly reports 20 cases.

W. S. REESE.

### Neurology

INTRA-OCULAR PHAKOMATA—A REPORT OF THREE CASES. R. F. LOWE, *Brit. J. Ophth.* 32:847 (Nov.) 1948.

Three cases of intraocular phakoma are recorded.

The appearance of the retinal phakomas in the 2 patients with Bourneville's disease (tuberous sclerosis) was so characteristic that diagnosis could have been made if these had been the only stigmas found. The diagnosis of the probable choroidal neurofibroma depends on the presence of numerous, widespread neurofibromas readily identified elsewhere, with bilateral secondary optic nerve atrophy, epilepsy and amentia. On appearances alone it could not be differentiated from other choroidal tumors.

W. ZENTMAYER.

### Ocular Muscles

OPERATIVE TREATMENT OF VERTICAL TROPIAS. B. F. PAYNE, *Am. J. Ophth.* 31:1217 (Oct.) 1948.

Payne concludes that planned operations for the relief of vertical tropias are successful if the diagnosis is correct. A clear understanding of the muscle or muscles involved is necessary, and the type and extent of operation are determined by the points brought out in the complete examination.

W. S. REESE.

INFLUENCE OF TORSIONAL MOVEMENTS ON THE AXIS OF ASTIGMATISM. S. VAN WIEN, *Am. J. Ophth.* 31:1251 (Oct.) 1948.

Van Wien discusses the influence of torsional movements on astigmatism. He suggests a test for cyclophoria in all cases of high astigma-

tism and, if the condition is present, the determination of the astigmatic axes binocularly by means of polaroid filters in the trial frame and over some of the test letters.

W. S. REESE.

### Physiology

THE RESPIRATION OF THE STORED CORNEA. T. D. DUANE, *Am. J. Ophth.* 31: 1400 (Nov.) 1948.

Duane draws the following conclusions from his study of bovine corneas:

1. Respiration studies have been made on bovine corneas stored from one and one-half hours to sixty days, under five conditions: intact eyes stored (1) above Ringer's solution at 4 C. and (2) under oil at 15 C.; isolated corneas stored in 5 per cent and 35 per cent solution of formaldehyde U. S. P., (3) in the "deep freeze" at 40 C. and (4) in the "deep freeze" after quick freezing.

2. The oxygen consumption rate ( $QO_2$ ) stored over Ringer's solution or under oil at low nonfreezing temperatures remains normal for seven days. The respiratory rate falls to one-fifth normal in ten to twelve days under these conditions.

3. Solution of formaldehyde U.S.P. inhibits respiration of the cornea immediately, and this is apparently irreversible.

4. The oxygen consumption of the cornea is reduced immediately to one-fifth normal by quick freezing and drops to this level within four days when kept at — 40 C. There is no further respiratory depression up to sixty days of storage.

W. S. REESE.

EFFECT OF MUSCULAR EXERCISE ON DARK ADAPTATIONS. J. P. WENDLAND, *Am. J. Ophth.* 31: 1429 (Nov.) 1948.

Wendland found that light exercise had essentially no effect on the rate of dark adaptation but that heavy exercise produced a tendency to elevation of the thresholds of the total dark adaptation curve and caused a decided biphasic response in final rod thresholds.

W. S. REESE.

### Retina and Optic Nerve

OPTIC NEUROPATHIES: A SIMPLIFIED CLASSIFICATION AND OUTLINE FOR ETIOLOGIC DIAGNOSIS. A. C. WOODS, *Am. J. Ophth.* 31: 1053 (Sept.) 1948.

Primarily from the etiologic viewpoint, Woods divides diseases of the optic nerve into two general classes: (1) degenerations of the optic nerve secondary to ocular disease, circulatory failure, local malformations and local accidents or infections and degenerations, with a hereditary basis, and (2) diseases of the optic nerve due to disease of the central nervous system, intracranial anomalies, systemic disease and various intoxications. A concise description of the various disorders of the optic nerve is given. The author insists that the ophthalmologist manage the case until its exact nature is decided on.

W. S. REESE.

HISTOLOGY OF THE RETINA IN A CASE OF TAY-SACHS'S DISEASE.  
J. A. MACMILLAN, *Am. J. Ophth.* 31: 1567 (Dec.) 1948.

MacMillan reports a case of amaurotic familial idiocy, including the pathologic changes. He suggests that one look for metabolic abnormalities and states the belief that the abnormal material in the ganglion cells is the result of an inherited metabolic dyscrasia.

W. S. REESE.

SCLERAL RESECTION IN THE TREATMENT OF RETINAL DETACHMENT:  
A PRELIMINARY REPORT. S. PHILPS, *Brit. J. Ophth.* 32: 811 (Nov.) 1948.

Philps reports 2 cases of retinal detachment successfully treated by scleral resection. A man aged 59 had a detachment of the retina following a blow on the right eye. After two diathermy operations the detachment was total. In the left eye a cataract had developed ten years previously. An intracapsular extraction was done and the retina was found to be detached. A diathermy operation was performed but was unsuccessful. Later a scleral resection was made. Five months later the retina was still in place; "the field was quite good," and vision was 5/60. A child 10 years of age had a detachment of the retina following a blow. A diathermy operation resulted in replacement of the retina, but nine months later a total detachment occurred. A scleral resection was then done and resulted in replacement of the retina. On last examination vision was "poor," as the macula had been involved in the detachment.

W. ZENTMAYER.

### Therapeutics

USE OF BACITRACIN IN OCULAR INFECTIONS. J. G. BELLOWES and C. J. FARMER, *Am. J. Ophth.* 31: 1211 (Oct.) 1948.

Bellows and Farmer found bacitracin well tolerated by the intact eye when applied topically as a fine powder or in saline solutions containing 1,000 to 5,000 units per cubic centimeter. The former solution did not appreciably delay regeneration of corneal epithelium, but the latter solution definitely retarded epithelial regeneration, with subsequent vascularization and scarring of the cornea. Bacitracin penetrated the injured and inflamed cornea, but not the normal cornea. Experimentally produced infections of the cornea and vitreous with a bacitracin-sensitive hemolytic *Staphylococcus aureus* were prevented when treated sufficiently early with bacitracin.

W. S. REESE.

ANTISTINE IN OCULAR ALLERGY. P. HURWITZ, *Am. J. Ophth.* 31: 1409 (Nov.) 1948.

Hurwitz briefly reviews the antihistaminic clinical drugs and presents 50 cases of ocular allergy and their response to antistine® (2-phenylbenzylaminomethyl-imidazoline), a new antihistaminic ophthalmic solution. He advocates its use.

W. S. REESE.

### Trachoma

THE ANTITRACHOMA CAMPAIGN IN JEWISH SCHOOLS OF JERUSALEM.  
B. MIRENBURG, *Am. J. Ophth.* 31: 1289 (Oct.) 1948.

Mirenburg describes the antitrachoma campaign in Jerusalem and gives tables showing the incidence, distribution and control of trachoma.

W. S. REESE.

INVOLVEMENT OF THE CANALICULI IN TRACHOMA. A. TZAREVA, *Vestnik oftal.* 26: 34, 1947.

Inflammation of the canaliculi is considered as a latent and recurrent source of trachomatous infection and as threatening to the corneal infection.

Tzareva examined all trachomatous patients of the Kirghiz eye clinic during the period from 1938 to 1945, paying special attention to infection of the canaliculi. In 53 patients, or 5.7 per cent, dacryocanaliculitis was observed, an enlarged punctum being usually present. In all these patients, the course of the trachomatous process as a rule was severe, with extensive pannus, corneal ulcers and, consequently, decreased vision in all eyes, with blindness in some. The method of treatment consisted in incising the canaliculi; this led to disappearance of the infection in 37 patients, while extirpation of the sac had to be resorted to in others. Thus, Tzareva urges the systematic examination of the canaliculi in order to prevent a focus of reinfection in trachomatous patients.

O. SITCHEVSKA.

### Tumors

MELANOBLASTOMA OF THE HUMAN CHOROID CULTURED IN VITRO:  
REPORT OF FOUR CASES. F. VRABEC, *Ophthalmologica* 115: 129  
(March) 1948.

Using the method of Carrel, the author obtained tissue cultures of 4 melanoblastomas of the human choroid and demonstrated the invasion of the tumor cells into the retinal tissue.

H. P. KIRBER.

A RARE CASE OF MULTIFORM GLIOBLASTOMA SPONGIOBLASTOMA OF  
THE RETINA. A. LOTIN, *Vestnik oftal.* 26: 65, 1947.

A child aged 2 years was brought into the clinic, where the diagnosis of a cataract of the right eye was made. Five months later iritis developed in that eye, and on the next visit, three months later, there was marked buphthalmos with a questionable tumor of the eye. Enucleation was performed, and microscopic examination revealed a rare histologic picture. There were characteristic degenerative pseudorosettes, with radial accumulation of the nuclear cells around the necrotic centers; anomalous giant cells and protoplasmic bodies with intensively stained nuclei. Young embryonic cells were evident. This picture was one of multiform spongioblastoma, or glioblastoma, of the retina, which Cushing found to constitute 30 per cent of gliomas of the brain.

O. SITCHEVSKA.

DIFFUSE MALIGNANT MELANOMA OF THE IRIS. S. RICHARDSON,  
Am. J. Ophth. 31:1223 (Oct.) 1948.

Richardson discusses malignant melanoma of the iris and reports 2 cases. He considers immediate enucleation the treatment of choice and does not think exenteration necessary.

W. S. REESE.

OSTEOMA INVOLVING THE ORBIT. F. W. NEWELL, Am. J. Ophth.  
31:1281 (Oct.) 1948.

Newell presents 7 cases of osteoma, the tumor arising in the ethmoid sinus in 2, in the sphenoid bone in 1 and in the frontal sinus in 4. The growths in the ethmoid sinus were removed, but the sphenoidal osteoma was considered inoperable and caused death from internal hydrocephalus.

W. S. REESE.



# Society Transactions

EDITED BY DR. W. L. BENEDICT

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COLLEGE OF PHYSICIANS OF PHILADELPHIA, SECTION ON OPHTHALMOLOGY

Perce DeLong, M.D., *Chairman*

M. Luther Kauffman, M.D., *Clerk*

*Regular Meeting, April 22, 1948*

**Heteroplastic Grafts: Presentation of a Case.** DR. O. A. CAPRIOTTI (by invitation) and DR. EDMUND B. SPAETH.

The patient presented was a 15 year old boy from the service of Dr. Spaeth at Wills Hospital on whom successful isografts had been performed for ectropion of the four eyelids complicating ichthyosis congenita.

He was an only child, and there was no history of abnormalities of the skin on either side of the family. Two weeks after his birth, a red rash appeared over the entire body, and this was soon followed by a generalized scaly condition of the skin. The diagnosis of ichthyosis congenita was established as a child, and he was presented by Dr. John Ludy at a dermatologic meeting.

Epiphora started at about the age of 8 years, and ectropion of the lids was rather severe at the age of 10. About four years previously the patient had been treated for one and a half years for a corneal ulcer of the left eye. Prior to admission he had been treated for three months as an outpatient for a corneal ulcer of the left eye, without benefit.

On general examination, the entire body of the patient was observed to be covered with brownish scales. The palms and soles were blackish and deeply fissured. The skin of the face was taut, and there was severe ectropion of both lower lids with slight ectropion of both upper lids. Photophobia and epiphora were pronounced. Examination with the slit lamp showed that the cornea of the right eye was clear, while the cornea of the left eye showed scarring just below the pupillary area and active ulcerative keratitis on the temporal side.

It was obvious that to correct the ectropion, which was the basic cause of the exposure keratitis, a skin graft would be necessary. But as the skin of the whole body was not normal and no members of the family were available, a skin donor was obtained. Patient and donor were of the same blood type and were cross matched as to blood type and M, N and Rh factors.

On Jan. 18, 1948, with the use of tribromoethanol solution anesthesia, a median tarsorrhaphy was performed on the patient's left eyelids. A linear incision was made parallel to the lid margin, and the skin was freed on either side. A free graft, taken from the donor's thigh, was fitted into the area, which had been prepared with thromboplastin solution. The lids were then covered with oiled silk and a firm pressure

bandage applied. The first dressing was done ten days later, and the isograft was found to be adherent, pink and free of discharge.

About twenty days later a similar operation was performed on the right eyelids, using the same donor. Ten days later, on first dressing, the graft was found to be adherent, pink and healthy.

Ectropion in patients with ichthyosis congenita is not a constant feature. According to the cases reviewed from the literature, the presence or absence of ectropion depends on the presence of the following factors: (1) involvement of the face and (2) atrophy of the skin, as well as on the degree and severity of the atrophy. The skin of the face atrophies and the skin of the eyelid retracts, thus causing eversion of the lid margins. Ectropion of all four lids is extremely rare, occurring only in severe cases; in such cases the patient usually dies in the first year of life.

Cases similar to the one presented, and with successful isografting, were reported by Elschnig (*Klin. Monatsbl. f. Augenh.* 1:17, 1912) and by Shimkin (*Brit. J. Ophth.* 29:363 [July] 1945).

In a review of the American literature no previously reported case of this type could be found.

#### DISCUSSION

DR. JAMES S. SHIPMAN: This case brings to my mind one I saw about ten years ago in which this operation should have been done, and was not. Indeed, it would have been fortunate for the patient if she could have had such an operation earlier in life. The patient was a white woman about 40 years of age who had made her living for many years as the "alligator woman" in a carnival. She had an extreme ichthyosis, and there was no mistake about her skin's looking like that of an alligator.

Dr. Spaeth is to be complimented on the excellent result in his case. I had the pleasure of seeing this boy at Wills Hospital before and after his operation, and the result was all that one could ask for. However, I should not destroy for at least another six months the beautiful adhesions holding these lids together. The boy is able to see to get around, and I should be concerned about these lids turning out again if they are cut too soon. I do not like to disagree with Dr. Spaeth, who has had much more experience with these cases than I have, but I feel that one must wait a long time before cutting these adhesions.

#### Follow-Up Studies in Five Cases of Intraocular Nonmagnetic Foreign Bodies. DR. JAMES S. SHIPMAN.

Six cases of intraocular copper foreign bodies were presented. Nearly sixteen, fifteen and thirteen years, respectively, had elapsed since operation in the first 3 cases. In cases 4 and 5, it had been over three years since operation. In case 6 the operation was done only one week prior to this report, and the patient was still hospitalized. In 5 cases the copper body was in the vitreous, and in 1 case it was in the anterior chamber. The first, third and fifth cases were similar in that the injuries were all incurred from coil winding machines at the same plant and the foreign body was a fine piece of copper wire. In the second and sixth

cases the injury was due to the explosion of a dynamite cap, and in the fourth case, to the explosion of a .22 caliber cartridge.

A technic was described for the removal of nonmagnetic foreign bodies from the vitreous and the anterior chamber respectively.

In the first 4 cases, all with copper in the vitreous, a posterior sclerotomy was done, and through the lips of the wound a small capsule forceps was inserted; while looking with the ophthalmoscope through the dilated pupil, the operator was able to grasp the foreign body in the vitreous and extract it through the sclerotomy opening. In the first case the scleral opening was closed with interrupted black silk sutures, without cauterization. In the other 3 cases the same method was employed, but the sclera was coagulated around the incision with diathermy, before suturing.

In the first case recovery was uneventful and vision was normal for five weeks after the operation. At the end of this time a retinal detachment was observed. This became more pronounced, and approximately two months after the original accident the first operation for retinal detachment was done with the Weve needles. This procedure was unsuccessful, and two more operations were performed, Safar pins being employed in the last. These attempts were also unsuccessful. At the time of the report, more than fifteen years after the patient's injury, the injured eye had no light perception, presented a complicated cataract and was divergent.

In the second case recovery was uneventful, and although the patient had a partial posterior cortical cataract, from the time he was first seen until almost fifteen years after the injury, he had had useful vision, 6/15 with correction. There was never any evidence of retinal detachment, and the visual field had remained full.

In the third case a more intense reaction followed operation than in the first two cases. The partial cataract which was present before operation became complete shortly afterward, and a linear extraction was necessary. After the cataract extraction, the patient made an uneventful recovery and had had no trouble since. At the time of the report, thirteen years after the injury, the eye was entirely quiet, with normal tension. The vitreous was clear, and the fundus was healthy, with no evidence of detachment. The visual field was full, and visual acuity of the injured left eye was 6/9 + with a + 13.00 D. sphere.

In the fourth case the prognosis was poor, owing to the very large foreign body and the massive preretinal hemorrhage which was present when the patient was first seen. A considerable amount of vitreous had been lost, and further hemorrhage occurred at the time of extraction of the foreign body. This hemorrhage persisted, and eventually the eyeball became phthisical. Enucleation of this eye was advised.

In the fifth case the copper wire was present in the anterior chamber. The wire was removed by means of a paracentesis made with a keratome and enlarged with scissors. The foreign body was then grasped with iris forceps and withdrawn. However, the iris became entangled and had to be replaced through the wound. This resulted in some incarceration, but no prolapse of the iris in the paracentesis wound. The pupil was pear shaped and drawn to the nasal side. A localized opacity still remained on the nasal side of the lens capsule. The media

were otherwise clear; the fundus was healthy, and both eyes were entirely quiet. At the last report, visual acuity, without correction was 6/5 in the right eye and 6/6 in the left eye.

The sixth, and last, case reported was one in which the nonmagnetic foreign body was localized in the vitreous and the same procedure was followed as in the other cases of nonmagnetic foreign bodies in the vitreous. However, in this case the results were much better than in the others, owing to the fact that after the sclerotomy opening had been made a bead of vitreous presented with the piece of copper glistening in the center of the bead. This was then extracted with forceps and the necessity of going any deeper into the vitreous was obviated. The scleral wound and the conjunctiva were then closed in the same manner as in the other cases. At the time of this report this patient was still hospitalized, and the outcome was uncertain.

*Comment.*—It was later realized that in the first case the eye should have been saved. The retinal tear made by the posterior sclerotomy should have been sealed off, and the detachment could have been repaired. Failure to do this was the result of lack of sufficient knowledge, sixteen years ago, of the method of closing retinal tears. In cases 2, 3 and 5 the results were as satisfactory as one could expect with such drastic surgical intervention. The situation in case 4 was considered unfavorable because of the large size of the foreign body and the massive preretinal hemorrhage. However, a larger sclerotomy might have been done earlier. It was realized in retrospect that an iridectomy should have been done in the fifth case.

The author stated that in his opinion the results obtained in the 5 reported cases of copper in the vitreous justify the technic used. However, a special type of forceps, such as a modification of the alligator forceps used by otologists, or a smaller and stronger forceps similar to those of Thorpe's, might aid in grasping and holding the foreign body. If the lens is too opaque for one to see the foreign body, the procedure described cannot be employed. However, since removal of the cataractous lens would be indicated, in any event, the extraction could be done first, followed by the technic described.

#### DISCUSSION

DR. GEORGE H. CROSS: Dr. Shipman has been fortunate in having cases in which the intraocular foreign body could be seen with the ophthalmoscope. Usually the lens is cataractous or the vitreous is filled with blood or exudate, through which it is impossible to see the foreign body. In such a case the foreign body is best removed with the aid of a biplane fluoroscope. With this method the foreign body is accurately localized roentgenologically.

Dr. Shipman was fortunate in having most of the foreign bodies small ones. He spoke of the use of the endoscope, which to my mind requires a large opening in the eyeball.

My experience with nonmagnetic foreign bodies is limited to about 100 cases, 50 of which were treated surgically. In many cases the localization was poor, or the foreign body was outside the eyeball. In 1 case it was localized in the lower conjunctival cul-de-sac. It is essential to have good localization of the foreign body.

If one has a good roentgenologic report, but cannot see the foreign body, and knows that it is nonmagnetic, one may try the biplane fluoroscope.

DR. EDMUND B. SPAETH: Dr. Cross has done a tremendous amount of work with the biplane fluoroscope. I know so little about the use of this instrument that it is perhaps unseemly of me to discuss it. I am not at all convinced that the biplane fluoroscope is good for the removal of nonmagnetic foreign bodies. The trauma done to the eye because of the mechanical difficulties connected with the use of the forceps without visualization of the operative field is too extensive for approval.

I wish to speak in greater detail about the use of the endoscope. I have had a fair amount of experience with this instrument and have found it valuable in cases in which it can be employed. Of course, one cannot use the endoscope when the vitreous is full of hemorrhage.

There are many factors connected with the removal of nonmagnetic metallic foreign bodies from the eye, and many different means of localization and extraction. Each individual case may require an individualized technic. At best, these cases frequently present difficult problems and should be studied in detail as to the method most applicable to the situation present. Dr. Shipman is to be congratulated on his results in these cases. The real tragedies in ophthalmology are the cases in which the foreign body could not be removed. I believe that every eye with a retained intraocular foreign body except for those of zinc and aluminum will be lost ultimately. With some substances, such as lead shot, the initial injury is so great that the eye is destroyed irrevocably at the start.

DR. JAMES S. SHIPMAN: With respect to the point that it was my good fortune that these foreign bodies could be seen, I do not feel that an opaque lens is a contraindication to this procedure. The lens must be removed anyway; then the foreign body can be seen and removed with the technic described.

I feel that, in order that a piece of copper be seen and removed by means of the biplane fluoroscope, the foreign body would have to be rather large, and in such a case the eye would be practically destroyed.

I doubt whether any of the foreign bodies in the cases I have described could have been seen well enough with the fluoroscope to warrant their removal by this method, since they were all unusually small pieces of copper.

**Relation of Cerebrovascular Resistance and the Grade of Retinal Changes in Hypertension.** DR. IRVING H. LEOPOLD, DR. SEYMOUR S. KETY (by invitation), DR. WILLIAM A. JEFFERS, DR. JOSEPH H. HAFKENSCHIEL (by invitation) and DR. HENRY A. SHENKIN.

Twenty-one hypertensive and 3 nonhypertensive subjects were studied, in an effort to find whether or not there was any correlation between the retinal vascular changes and the cerebrovascular resistance associated with hypertension. The cerebral blood flow was determined by the method of Kety and Schmidt, and the retinal vascular changes were evaluated according to the classification of Wagener and co-workers.

It was found that a statistically significant correlation existed between retinal changes and the cerebrovascular resistance. The relation was a direct one in that as cerebrovascular resistance increased, the grade of retinopathy also tended to increase.

It is evident that the retinal changes do reflect with some accuracy the state of the cerebral circulation, but the degree of accuracy is not high, in that one cannot predict from the ophthalmoscopic findings the exact extent to which the cerebrovascular resistance has been raised.

DR. SEYMOUR S. KETY: When the physiologist studies hypertension in man, he is impressed with the fact that practically everything he investigates proves to be normal. The output of the heart is normal; the blood flow through the kidney is essentially normal except in the very late stages; the blood flow through the skin, the periphery of the body and the muscles has always been found to be physiologic. If he calculates the resistance in the blood vessels of these various organs, he finds a uniform increase in the peripheral resistance throughout the body and in any individual organ. Since the brain has been implicated in numerous etiologic theories of hypertension, we thought it of great interest to study the cerebral blood flow, and finally a method was developed at the University of Pennsylvania which permitted such a determination. It was found that exactly the same amount of blood passes through the brain of the hypertensive patient as passes through the brain of a normotensive person. The interesting thing, however, was that this occurred even though the blood pressure might be twice the normal. This must indicate a high degree of resistance in the blood vessels of the brain that keeps back the flow of blood which otherwise would be much above the normal.

Dr. Leopold has discussed the possibility which that finding presented to him as an ophthalmologist—that now, with a method for quantitating the resistance in the brain, one could evaluate the clinical impression of clinicians and ophthalmologists that the changes in the eyegrounds are a reflection of what is going on in the brain. We were gratified to find that there was a fairly good correlation between the two; that the correlation is not better is not surprising, for one must remember that we were measuring the vascular resistance at one time, at the time of observation, and that resistance was a function of the degree of spasticity of the vessels at that particular moment. The changes in the eyegrounds according to the classification used not only are a measure of the degree of spasm in the vessels at that particular moment but also reflect how long that spasm has been going on, and how severe it is. These changes in the eyegrounds are the result not only of spasm, but of spasm over a long period of time. If it were possible to separate the various factors that enter into retinopathy, particularly the degree of hypertonus at the time of observation and the results of the past history of that tonus, one might get an even better correlation than the quite satisfactory one that Dr. Leopold has found.

DR. FRANCIS HEED ADLER: I should like to ask Dr. Leopold whether there is any difference in the cerebrovascular resistance in patients with atherosclerosis and that in patients with arteriolosclerosis. Dr. Leopold is evaluating the changes in the eyegrounds which admittedly are

severer in cases of arteriolosclerosis. It is possible that patients with atherosclerosis might have high cerebrovascular resistance and yet show no pathologic changes in the fundus. This state would upset the true correlation between cerebrovascular resistance and hypertensive retinopathy seen in cases of mild and rapidly progressive hypertensive vascular disease.

There are still many things which are not known about the retinal circulation. It has always been taught that the ocular vessels are end arteries, for they are said to be like the cerebral arteries. Until fairly recently, it was believed that the cerebral arteries were end arteries in the sense of Cohnheim. Lorente de Nó stated that the cerebral arteries are in no sense end arteries and that blood cells in the capillaries can pass freely from one end of the cerebral cortex to the other. It may be time that the retinal circulation be reinvestigated to determine whether there are anastomoses between the various branches of the retinal arterial tree.

DR. I. S. TASSMAN: It is difficult properly to digest and interpret in such a short time a presentation of this kind. A question occurs to me, especially with reference to the point that Dr. Adler introduced, "Is it possible to correlate findings of this kind for practical purposes?" The vascular beds in the two organs supplied, for example, are of different natures. There are differences in these structures, as well as possible differences in the arterioles of the brain and those of the retina.

In their origin, course and number, the cerebral vessels, with their ramifications, are quite different from the retinal vessels, so that a difference in the vascular resistance of the two sets of vessels might be expected. Is it possible, therefore, to correlate satisfactorily the resistance of the one with the pathologic changes in the other?

DR. IRVING H. LEOPOLD: The figures for normal cerebral blood flow are based mostly on values found in young persons between 20 and 30 years of age. The hypertensive patients studied here were also from a young age group, approximately 20 to 45, for the most part. In this group senile atherosclerosis would probably have a low incidence. The same cannot be said for local atherosclerosis. As yet no correlation of atherosclerotic change in retinal vessels with cerebrovascular resistance has been made.

The retinal and cerebral vessels differ in many ways. There is, for example, no cerebral counterpart of the crossing phenomenon of retinal vessels. Nevertheless, evidence has been presented in the past suggesting that the two systems of vessels show similar changes, and the present study also demonstrates a significant relation in the presence of hypertension.

## ANEURYSM OF THE POSTERIOR COMMUNICATING ARTERY

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THE growing interest in the clinical recognition of cerebral aneurysms, due largely to the promising possibilities of surgical treatment, demands elucidation of their characteristics for purposes of accurate diagnosis. For this reason we report a group of cases of aneurysm of the posterior communicating artery, in order to call attention to salient features for diagnosis, as well as to indicate the possibilities of treatment.

### REPORT OF CASES

*CASE 1.—History.*—C. S., a married man aged 59, a railroad car inspector, was admitted to the neurologic service of the Jefferson Hospital on April 18, 1947 with a history of having had the onset of right frontal headache seventeen days before admission. The headache was constant and was associated with buzzing in the head, ringing in the ears, impairment of vision and intermittent nausea. The headache gradually became more pronounced and ten days after onset was followed by vomiting and sudden severe pain behind the right eye and in the back of the neck. The pain persisted and was soon followed by drooping of the right eyelid. When the right eyelid was raised double vision was noted. The symptoms persisted until the patient's admission to the hospital.

The past medical history revealed that the patient had had typhoid in childhood and influenza in 1918. The family history revealed that the mother had had hemiplegia before her death, at the age of 84.

*Examination.*—General physical examination disclosed no abnormalities of the heart, lungs or abdomen. The blood pressure was 170 systolic and 90 diastolic.

Neurologic examination revealed ptosis of the right eyelid; right internal ophthalmoplegia and paralysis of upward, inward and downward gaze of the right eye; slightly faster patellar and achilles reflexes on the left, and slight nuchal rigidity.

*Laboratory Data.*—Urine was normal. Blood studies revealed 81 per cent hemoglobin, 4,600,000 red cells and 11,400 white cells. The Wassermann and Kahn reactions of the blood were negative. The urea clearance was 80 per cent. Studies of the spinal fluid revealed xanthochromia, a pressure of 150 mm., a negative Wassermann reaction and a total protein content of 70 mg. per hundred cubic centimeters. The electrocardiogram revealed a low voltage T wave in the limb leads, suggesting myocardial change. A roentgenogram of the chest showed cardiac enlargement, and a roentgenogram of the skull revealed no abnormality.

From the Department of Neurology, Jefferson Medical College.



*Comment.*—The history of onset with headache followed several days later by right oculomotor paralysis was so characteristic that a diagnosis of aneurysm of the right posterior communicating artery was made and craniotomy performed on May 5, 1947 by Dr. Rudolph Jaeger, without benefit of an arteriogram. An aneurysm of the right posterior communicating artery was disclosed and removed. Death occurred shortly after operation.

*CASE 2.—History.*—D. B., a white housewife aged 29, was first admitted to the neurologic service of the Jefferson Hospital on Dec. 10, 1946 and was subsequently readmitted on Jan. 15, 1947. The onset of the present illness occurred three weeks prior to admission to the hospital, when the patient felt a dull pain in and above the right eye. One week later she experienced a sudden sharp pain in the right side of her head, lasting only a few seconds, but within a few days severe, sharp pain reappeared behind the right eye and involved the entire right side of the head and face. The pain remained severe for two days and extended to involve the entire head, as well as the neck, arms and legs. As it subsided somewhat, drooping of the right eyelid appeared and was accompanied with double vision. The drooping of the eyelid increased rapidly to complete closure of the eye, which persisted, while the pain gradually diminished.

*Examination.*—General physical examination revealed no abnormalities of the heart, lungs or abdomen. The blood pressure was 130 systolic and 84 diastolic.

Neurologic examination revealed a relatively larger pupil on the right side, which reacted sluggishly to light and in accommodation; almost complete ptosis of the right eyelid; marked impairment of upward, inward and downward gaze of the right eye, and a relatively diminished right corneal reflex.

*Laboratory Data.*—The urine was normal. Blood studies revealed 75 per cent hemoglobin, 3,800,000 red cells and 9,200 white cells. The Wassermann and Kahn reactions of the blood were negative. Spinal fluid studies revealed a clear and colorless fluid, with red blood cells observed on microscopic examination. The spinal fluid pressure was 200 mm., and the Wassermann reaction was negative. A roentgenogram of the skull showed no abnormalities. A cerebral arteriogram of the right internal carotid artery showed no evidence of an intracranial aneurysm (fig. 1).

*Comment.*—In view of the characteristic onset and course of the illness, a presumptive diagnosis of intracranial aneurysm involving either the right internal carotid artery or the right posterior communicating artery was made, despite the normal arteriogram. Craniotomy was performed on January 20 by Dr. Rudolph Jaeger, and a saccular aneurysm originating from the right posterior communicating artery was revealed. Although the aneurysm ruptured on removal, it was extirpated completely after proximal and distal ligation. Prior to operation there had been definite evidence of improvement of function of the right oculomotor nerve, as shown by diminished ptosis and increased movement of the eye. After operation there was a recurrence of paralysis of the right oculomotor nerve. Recovery was uneventful except for this, and the patient was discharged on February 12.

*CASE 3.—History.*—N. T., a Negro woman aged 36, was referred from the Wills Hospital to the neurologic service of the Jefferson Hospital on Oct. 16, 1946. The onset of the present illness occurred on August 30, six weeks before her admission, when the patient had a lower tooth extracted on the right side. Five days later, while on her way to work, she suddenly experienced a severe headache in the region of the vertex, with extension into the back of the neck. The headache persisted for a week, was partially relieved by medication and was increased by movement of the head. As the headache gradually subsided, it was replaced by

a dull pain in and around the left eye; this pain persisted and was followed within a day or two by drooping of the left eyelid. The ptosis increased rapidly within two days to the point of complete closure of the left eye. The drooping of the left eyelid persisted, but the pain in the left eye subsided gradually over a period of about two weeks. The family and past medical histories were not pertinent to her present problem.

*Examination.*—General physical examination revealed no abnormalities of the heart, lungs or abdomen. The blood pressure was 110 systolic and 60 diastolic.

Neurologic examination revealed the following significant changes: a relatively larger pupil on the left side, which failed to react to light or in accommodation; almost complete ptosis of the left eyelid; external strabismus of the left eye with inability to move the left eye upward, inward and downward except for slight



Fig. 1 (case 2).—Normal arteriogram in a proved case of aneurysm of the posterior communicating artery.

counterclockwise rotary movement on attempted downward gaze; equally active corneal reflexes, and no disturbance of sensation over the face.

*Laboratory Data.*—Urine was normal. Blood studies revealed 78 per cent hemoglobin, 4,100,000 red cells and 6,000 white cells. The Wassermann and Kahn reactions of the blood were negative. Spinal fluid studies revealed a clear and colorless fluid, under 95 mm. of pressure, 1 cell per cubic millimeter, a negative Wassermann reaction and a colloidal gold curve of 0000000000. The electrocardiogram was normal. Roentgenograms of the chest and the skull showed no abnormalities. A cerebral arteriogram of the left internal carotid artery was suggestive of a small aneurysm of the left posterior communicating artery (fig. 2).

*Comment.*—Because of the characteristic history and the evidence of a progressive paralysis of the left oculomotor nerve, as well as possible involvement of

the left trochlear nerve, a presumptive diagnosis of intracranial aneurysm originating either from the left posterior communicating artery or from the left internal carotid artery was made. A craniotomy was performed on Dec. 4, 1946 by Dr. Rudolph Jaeger, and a small saccular aneurysm was discovered attached to the left posterior communicating artery. Proximal ligation and obliteration of the aneurysm were carried out, after which the patient made an uneventful recovery. Both at the time of discharge, on December 15, and on subsequent observation no evidence of recovery of function of the left oculomotor nerve was disclosed.

**CASE 4.—History.**—M. B., a Negro woman aged 34, was referred from the Wills Hospital to the neurologic service of the Jefferson Hospital on June 17, 1946 with a history of having had occasional pain beneath the left eye for three or four years. The pain was considered to be neuralgia and was relieved by acetylsalicylic acid. One month before admission the patient was awakened



Fig. 2 (case 3).—Arteriogram demonstrating aneurysm of the left posterior communicating artery.

during the night by a severe pain in the left occipital region, the pain extending forward over the left side of the head into the left eye. The severe pain persisted for three days and subsided gradually over a period of three weeks, a process which was associated with drooping of the left eyelid and double vision. The drooping of the eyelid increased to the point of complete closure after three days. The family and past medical histories were without significance.

General physical examination revealed no abnormalities of the heart, lungs and abdomen. The blood pressure was 110 systolic and 70 diastolic.

Neurologic examination revealed the following significant changes: a relatively larger pupil on the left, with both pupils reacting well to light and in accommodation; almost complete ptosis of the left eyelid; slight external strabismus of the left eye and marked limitation of movement of the left eye upward, inward and

downward; equally active corneal reflexes, and no disturbance of sensation over the face.

*Laboratory Data.*—The urine was normal. Blood studies revealed 71 per cent hemoglobin, 4,200,000 red cells and 9,600 white cells. The Wassermann and Kahn reactions of the blood were negative. The spinal fluid was clear and colorless, with a pressure of 120 mm.; studies revealed less than 1 cell per cubic millimeter, a negative Wassermann reaction and a colloidal gold curve of 0001221000. A roentgenogram of the skull showed no abnormalities (fig. 3).

*Comment.*—On the basis of the characteristic onset and course of the illness, as well as the evidence of ophthalmoplegia in the distribution of the left oculomotor, and possibly the left trochlear, nerves, a presumptive diagnosis of intracranial aneurysm involving either the left internal carotid artery or the left posterior communicating artery was made. A craniotomy was performed on July 3, 1946 by Dr. Rudolph Jaeger, and a small saccular aneurysm was revealed, taking its

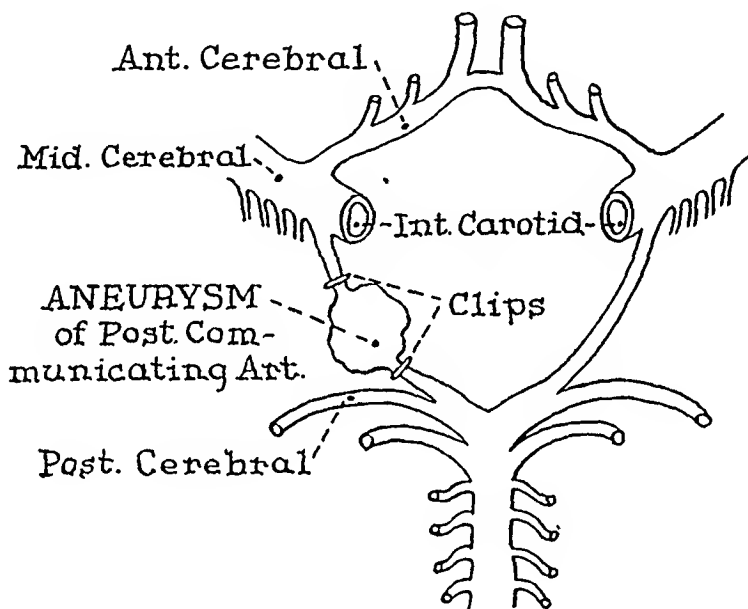


Fig. 3 (case 4).—Aneurysm of the left posterior communicating artery, shown in diagram.

origin from the left posterior communicating artery. The aneurysm was removed after proximal and distal ligation. The operation was followed by persistence of the complete paralysis of the left oculomotor nerve which was still present when the patient was discharged on July 16. Subsequently, there was progressive return of function of the left oculomotor nerve, and after several months no evidence of weakness of the extraocular muscles could longer be detected.

*CASE 5.—History.*—C. F. M., a woman aged 43, a telephone operator, was admitted to the medical service of the Jefferson Hospital on May 23, 1946. The onset of the present illness occurred suddenly at about 1 a. m., five days before admission, when the patient awoke from her sleep with a headache. She was able to fall back to sleep, but four hours later she again awoke with a severe headache, which was generalized and dull in character. The headache persisted and on the day of admission became much more pronounced during the afternoon. At that time there was also noted sharp, lancinating pain in the right eye, associated with bright flashes of light in the visual field of that eye. Within a half-hour other

symptoms developed in the form of generalized weakness, perspiration, nausea, vomiting and pain the back. The past medical history revealed that the patient had had a chronic infection of the ear, with intermittent drainage affecting both ears, for fifteen years, with resultant impairment of hearing. The family history was without significance.

*Examination.*—General physical examination showed no abnormalities of the heart, lungs or abdomen. The blood pressure was 110 systolic and 70 diastolic. Examination of the ears showed chronic otitis media bilaterally.

Neurologic examination revealed nuchal rigidity, a bilateral Kernig sign and slight weakness of upward and inward gaze of the right eye. Within a few days the weakness of the extraocular muscles of the right eye progressed to the point of complete paralysis of the right oculomotor nerve, including ptosis and a dilated pupil, which failed to react to light or in accommodation. Subsequently, over a period of about two weeks, there was diminution in ptosis of the right eye, and the right pupil, although still dilated, showed a reaction to light and in accommodation. The headaches persisted. Craniotomy was performed on June 17 (fig. 4).

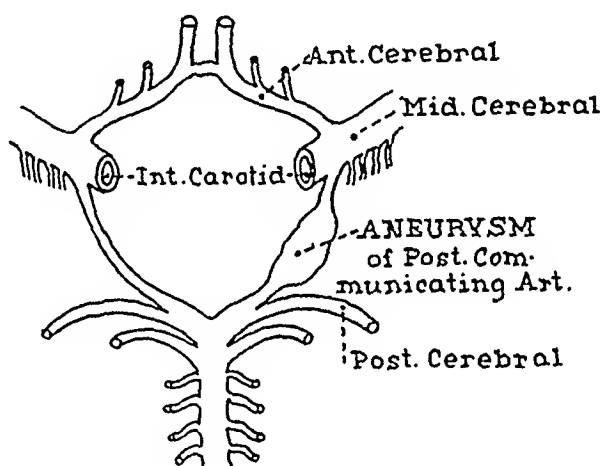


Fig. 4 (case 5).—Aneurysm of the right posterior communicating artery, shown in diagram.

*Laboratory Data.*—The urine was normal. Blood studies revealed 84 per cent hemoglobin, 4,160,000 red cells and 9,950 white cells. The Wassermann and Kahn reactions of the blood were negative. The spinal fluid was under increased pressure of 215 mm. and was grossly bloody. A roentgenogram of the skull was normal except for evidence of mastoid infection bilaterally.

*Comment.*—Craniotomy revealed a saccular aneurysm of the right posterior communicating artery at the edge of the tentorium with discoloration of the surrounding dura. During the operation the aneurysm, which was about 1 cm. in diameter, ruptured but was ultimately removed after proximal and distal ligation. Immediately after operation the patient had left hemiplegia, as well as complete paralysis of the right oculomotor nerve. The hemiplegia subsided, but the right oculomotor nerve palsy was still present at the time of discharge, on July 16, 1946.

*CASE 6.—History.*—A. L. R., a Negro woman aged 60, was referred from the Wills Hospital to the neurologic service of the Jefferson Hospital on Feb. 24, 1946, with a history of having awakened one morning seven weeks before admission

to discover slight drooping of her left eyelid. Within a few hours the drooping of the eyelid had increased to the point of complete closure of the eye. At no time did she experience headache or any other symptoms referable to the nervous system. The family and past medical histories were noncontributory.

*Examination.*—General physical examination revealed a functional systolic murmur but no other abnormalities of the heart, lungs or abdomen. The blood pressure was 130 systolic and 70 diastolic.

Neurologic examination revealed the following significant changes: retinal choroiditis bilaterally with some narrowing and increased tortuosity of the smaller retinal arterioles; a dilated left pupil, which failed to react to light or in accommodation, and a smaller right pupil, which reacted well to light and in accommodation; complete ptosis of the left eyelid; external strabismus of the left eye with inability

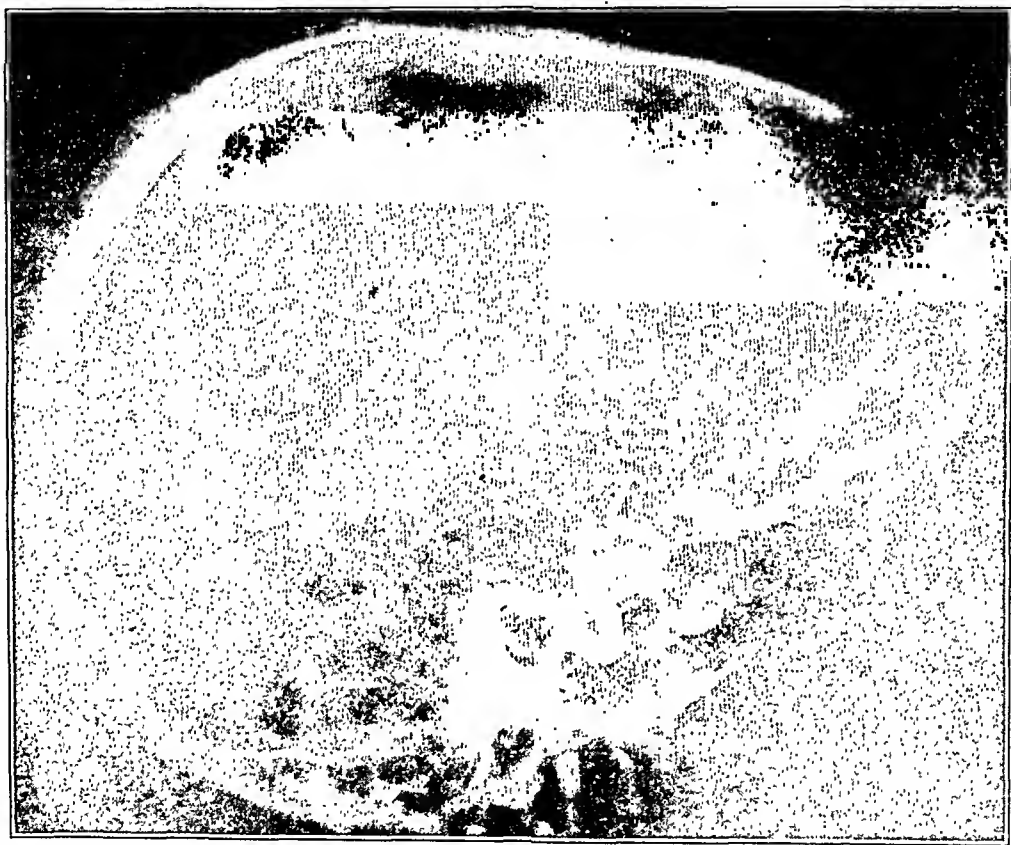


Fig. 5 (case 6).—Normal arteriogram in a case of aneurysm of the posterior communicating artery.

to move the left eye upward, inward and downward, and equally active corneal reflexes.

*Laboratory Data.*—The urine was normal. Blood studies revealed 58 per cent hemoglobin, 3,100,000 red cells and 5,600 white cells. The Wassermann and Kahn reactions of the blood were negative. The blood urea nitrogen was 9.8 mg. and the blood sugar 80 mg. per hundred cubic centimeters. The protein level of the spinal fluid was 58 mg. per hundred cubic centimeters, but the fluid was otherwise normal. The electrocardiogram showed a left axis deviation but no other abnormalities. A roentgenogram of the chest showed some widening of the aortic arch. A roentgenogram of the skull was normal. Cerebral arteriography revealed no evidence of an intracranial aneurysm (fig. 5).

*Comment.*—In view of the course of illness, which was characterized by the sudden onset of partial paralysis of the left oculomotor nerve and possibly involvement of the left trochlear nerve, a presumptive diagnosis of an intracranial aneurysm involving either the left internal carotid artery or the left posterior communicating artery was made, despite the absence of headache and the normal appearance of the arteriogram. A craniotomy was performed on March 27, 1946 by Dr. Rudolph Jaeger, and a saccular aneurysm was disclosed originating in the left posterior communicating artery near its junction with the left internal carotid artery. It was impossible to remove the aneurysm successfully, and treatment was limited to both intracranial and cervical ligation of the left internal carotid artery. Death occurred three days after operation. Autopsy was not allowed.



Fig. 6.—Aneurysm of the right posterior communicating artery and a small aneurysm of the right middle cerebral artery.

**CASE 7.—History.**—M. R., a white woman aged 58, was admitted to the neurologic service of the Jefferson Hospital on Sept. 21, 1947. For many years she had suffered from headaches confined to the right side of the head, which occurred at intervals of two to four weeks and were associated with nausea and vomiting. These attacks had been regarded as typical migraine headaches and, indeed, appeared to have all the features of such headaches. Two weeks before admission to the hospital she experienced sudden, persistent pain behind the right eyeball. She had no further symptoms except for the constant retro-orbital pain on the right side, which defied relief. One week after its appearance she suddenly experienced a "bursting sensation" in her head during a trying telephone conversation held in her capacity as secretary to a physician. The headache was intense and was followed by slight

drooping of the right eyelid and diplopia. With the persistent and constant headache there developed in the course of twenty-four hours complete ptosis of the right eyelid and inability to rotate the right eyeball, associated with diplopia. At this time she entered the hospital for study.

*Neurologic Examination.*—The patient was profoundly prostrated. Examination revealed pronounced nuchal stiffness and a bilateral Kernig sign; complete ptosis of the right eyelid with inability to rotate the right eyeball upward, inward or downward, and a grossly bloody spinal fluid.

*Laboratory Data.*—The urine was normal. Blood count showed 3,940,000 red cells, 8,200 white cells and 71 per cent hemoglobin. The blood urea nitrogen was 22.8 mg. per hundred cubic centimeters and the urea clearance 140 per cent. The Wassermann and Kahn reactions of the blood were negative. The spinal fluid was clear, with a pressure of 130 mm., protein content of 25 mg. per hundred cubic centimeters, 3 cells per cubic millimeter, a negative Wassermann reaction and a normal colloidal gold curve. The electrocardiogram revealed a mild left axis deviation but was otherwise normal. A roentgenogram of the skull revealed no abnormalities.

*Comment.*—This case reveals several pertinent problems associated with the problem of aneurysm. The long-standing history of hemi-crania suggestive of migraine is not infrequently encountered in any extensive experience with aneurysm. The development of the illness, leading to hospitalization, was characteristic of a ruptured aneurysm and was associated with intense headache, signs of meningeal irritation and cranial nerve palsy. Finally, the problem of treatment was well illustrated by this case. Because of the clear evidence of rupture and subarachnoid hemorrhage and the indications of profound prostration, operation was not undertaken. The patient died shortly after entering the hospital, and autopsy revealed a ruptured aneurysm of the right posterior communicating artery and an unruptured small aneurysm of the right middle cerebral artery (fig. 6).

#### GENERAL COMMENT

*Incidence.*—Aneurysms involving the posterior communicating artery are said to be rare, but the present series of 7 verified cases indicates that they are not as rare as they seem. Dandy<sup>1</sup> was unable to discover a single case in his series of 133 verified aneurysms. He explained the disparity between his observations and those of others by the fact that careful dissection of the aneurysms indicated that they actually arose from the internal carotid artery. Our observations demonstrate that aneurysms may involve the posterior communicating artery alone, without taking origin from the internal carotid artery. Of 1,025 verified cases of aneurysms from the literature, McDonald

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1. Dandy, W.: Intracranial Arterial Aneurysm, Ithaca, N. Y., Comstock Publishing Company, Inc., 1945.



and Korb<sup>2</sup> found the posterior communicating artery involved in 66. Aneurysms of this artery were reported by Gall<sup>3</sup> who found 4 in a series of 62 aneurysms; by Lebert<sup>4</sup> who found 7 among 86 aneurysms; by Epron,<sup>5</sup> who reported 4 in a series of 89 aneurysms, and by Hey,<sup>6</sup> Reinhardt,<sup>7</sup> Symonds,<sup>8</sup> Berger<sup>9</sup> (2 cases), Hassin,<sup>10</sup> Shore,<sup>11</sup> Schmidt<sup>12</sup> (2 cases), Sands,<sup>13</sup> Dassen,<sup>14</sup> Kersley,<sup>15</sup> Krayenbühl,<sup>16</sup> Fattovich,<sup>17</sup> Keegan and Bennett,<sup>18</sup> Strauss, Globus and Ginsburg,<sup>19</sup> Dial and Maurer,<sup>20</sup> Frazier<sup>21</sup> and Elmer and Baylon.<sup>22</sup>

*Clinical Features.*—The clinical features of aneurysm of the posterior communicating artery are similar to those of aneurysm involving other

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9. Berger, W.: Ueber Aneurysmen der Hirnarterien, Virchows Arch. f. path. Anat. **245**:138, 1923.

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11. Shore, B. R.: Intracranial Aneurysms, Arch. Neurol. & Psychiat. **21**:607 (March) 1929.

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14. Dassen, R.: Ophthalmic Migraine and Aneurysm, Semana méd. **1**:1049, 1931.

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16. Krayenbühl, H.: Das Hirnaneurysmen, Schweiz. Arch. f. Neurol. u. Psychiat. **47**:155, 1941.

17. Fattovich, G.: Contribution to the Study of Intracranial Aneurysms, Note e riv. di psichiat. **69-71**:433, 1940-1949.

18. Keegan, J. J., and Bennett, A. E.: Cerebral Aneurysm and Cortical Herniation, Arch. Neurol. & Psychiat. **26**:36 (July) 1931.

19. Strauss, I.; Globus, J. H., and Ginsburg, S. W.: Spontaneous Subarachnoid Hemorrhage, Arch. Neurol. & Psychiat. **27**:1080 (May) 1932.

20. Dial, D. L., and Maurer, G. B.: Intracranial Aneurysms, Am. J. Surg. **35**:2, 1937.

21. Frazier, C. H.: Clinical and Pathological of Parahypophyseal Lesions: A Review, Surg., Gynec. & Obst. **62**:1, 1936.

22. Elmer, A. F., and Baylon, C. E.: Cerebral Aneurysms, M. Rec. **135**:577, 1932.

portions of the circle of Willis. The typical instance is characterized by headache, usually unilateral and often recurrent, followed after a varying period by ophthalmoplegia involving the oculomotor nerve to a varying degree. The headache may persist for only five days (case 5), or it may last for six weeks (case 3); in other instances it may be present intermittently for months, or there may be a background of what is usually regarded as migraine for many years (case 7). The onset may be with paralysis of the oculomotor nerve (case 6), but usually the oculomotor paralysis follows the headache, either immediately or after an interval of hours or days. In still other instances rupture of the aneurysm ushers in the disease (case 7). The headache is almost always unilateral, on the same side as the aneurysm, and is associated with pain in and above the eyeball on the affected side (cases 1, 2, 3, 4 and 5). In cases in which the pain begins in other parts of the head, it settles eventually in the eyeball (case 3), and at times it involves the entire side of the head (cases 2 and 7).

There is nothing in the headache which distinguishes aneurysm of the posterior communicating artery from aneurysm elsewhere in the brain. It is the oculomotor paralysis which indicates involvement of the vessel in question because of the intimate anatomic relation of the oculomotor nerve to the posterior communicating artery. Unfortunately, aneurysm involving the internal carotid artery may cause oculomotor paralysis, but in this case there is often involvement of the optic nerve or of other adjacent cranial nerves. If, in a suspected case of intracranial aneurysm, there is isolated paralysis of the oculomotor nerve or paralysis of the oculomotor nerve with associated paralysis of the trochlear nerve, the probabilities favor aneurysm of the posterior communicating artery.

The practical point at issue is that aneurysm of the posterior communicating artery is usually smaller than that of the internal carotid artery and is therefore more accessible to ligation. There were 3 deaths among the 7 cases reported, but in case 7 the patient entered the hospital in profound prostration due to rupture of the aneurysm. Aneurysms of the posterior communicating artery are small, are usually accessible to ligation and constitute, therefore, a favorable type of cerebral aneurysm. Ligation may be followed by recession of the paralysis of the oculomotor nerve or there may be no change whatever in the ophthalmoplegia. In either case the primary object of ligation, prevention of rupture of the aneurysm, will have been accomplished.

#### DIAGNOSIS

Aneurysm of the posterior communicating artery must be considered a good possibility in a subject with recurrent headache, followed by oculomotor paralysis of varying degree. Little can be expected from

roentgenologic studies, since erosion of the skull is not usual. Some help may be obtained from the presence of retinal arteriosclerosis and/or roentgenologic evidence of calcification of the internal carotid arteries. These signs will not establish the diagnosis, but they may confirm it. The spinal fluid is normal except in those rare instances in which syphilis is the cause of the aneurysm, and in the more frequent circumstances of rupture of the aneurysm, when bloody or xanthochromic spinal fluid is found. There is little in the systemic examination which is significant in the usual case. Hypertension helps little in the diagnosis, except to raise the possibility of an aneurysm associated with arteriosclerosis, but most aneurysms are not associated with changes in the blood pressure. Endocarditis may raise the issue of mycotic aneurysm, also a rare possibility. In the last analysis, the clinical history and the demonstration of ophthalmoplegia referable to the third nerve will be the most important factors in the diagnosis of an unruptured aneurysm of congenital origin. The diagnosis may be established with certainty by arteriographic examination, but in almost all cases this procedure is unnecessary for the establishment of the diagnosis.

#### CONCLUSION

A series of 7 cases of aneurysm of the posterior communicating artery alone is reported.

The clinical history of recurrent headache associated with the development of ophthalmoplegia involving the third nerve appears to be the most significant feature in the diagnosis. There is little else which has been found to be helpful, except for the arteriogram.

In 4 of 6 cases operation was successful. In the seventh case death occurred before operation could be accomplished.

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# PENETRATION OF AUREOMYCIN INTO THE EYE

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THE EFFECTIVE use of aureomycin in treatment of several external infections of the eye has been reported by Braley.<sup>1</sup> Because of the possibility that aureomycin may be of value also for intraocular infections, the current study was undertaken to determine the penetration of this new antibiotic into rabbit eyes following various methods of administration.

## TECHNIC

*Topical Application.*—The technic as described by von Sallmann<sup>2</sup> was used in iontophoresis, the corneal bath and subconjunctival injection. A fresh solution of 0.5 per cent aureomycin borate was made daily, distilled water being used as the solvent. After production of local anesthesia with 6 drops of 0.1 per cent dibucaine hydrochloride (nupercaine hydrochloride®), the applicator tube was filled to the halfway mark (2.5 to 3.0 cc. of solution). At the end of the procedure the excess fluid was carefully removed, and about 0.25 cc. of aqueous was withdrawn at stated intervals with a 27 gage needle on a tuberculin syringe. The amount of aqueous removed varied occasionally, depending on the size of the anterior chamber. In the iontophoresis experiment 1.6 milliamperes was employed with the cathode on the eye and the anode on the head of the animal. Anode iontophoresis was first tried but was abandoned because it caused excessive damage to the eye. One drop of fluorescein sodium was applied to the corneas four, twenty-four and, if necessary, forty-eight hours after treatment.

In the experiment with subconjunctival injection, 0.5 per cent aureomycin borate was dissolved in sterile distilled water or in 0.5 per cent procaine hydrochloride. When higher concentrations of procaine were used, aureomycin borate did not readily go into solution. After production of local anesthesia with drops of 0.1 per cent dibucaine hydrochloride, 0.5 cc. of the procaine-aureomycin solution was injected subconjunctivally in the region of the superior rectus muscle and 0.25 cc. of aqueous was withdrawn at stated intervals. The concentration of aureomycin in the aqueous was measured by the serial dilution method, as described by Dornbush,<sup>3</sup> and the end point was read at four hours. Since Dornbush's test

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The aureomycin for these experiments was obtained from Lederle Laboratories Division, American Cyanamid Company, Pearl River, N. Y.

From the Department of Ophthalmology, Columbia University College of Physicians and Surgeons, and the Institute of Ophthalmology, Presbyterian Hospital.

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2. von Sallmann, L., and Meyer, K.: Penetration of Penicillin into the Eye. Arch. Ophth. **31**:1 (Jan.) 1944; Penetration of Penicillin into the Eye: Further Studies, *ibid.* **34**:195 (Sept.) 1945.

3. Dornbush, A. C., and Pelcak, E. J.: Determination of Aureomycin in Serum and Other Body Fluids, Ann. New York Acad. Sc. **51**:218 (Nov.) 1948.

requires at least a 1 cc. sample, the method had to be modified by using correspondingly smaller amounts of all solutions.

*Systemic Administration.*—Aureomycin hydrochloride, dissolved in distilled water, was given intravenously, intramuscularly and orally. For the intravenous and intramuscular procedures, 20 mg. of aureomycin hydrochloride per kilogram of body weight, dissolved in 5 cc. of distilled water, was injected into the ear vein and thigh muscles, respectively.

For the oral method, 50 mg. per kilogram of aureomycin hydrochloride in distilled water was administered, in the use of a wooden gag and a rubber stomach tube, the aureomycin being washed down with water to prevent any of the solution from remaining in the tube.

The animals were killed at various intervals by intravenous injection of pentobarbital sodium (nembutal®). Heart blood was taken; the eyes were enucleated, and a cisternal puncture was made in an attempt to obtain spinal fluid. The aqueous was then withdrawn and the eyes were dissected. The wet cornea, sclera,

TABLE 1.—*Aureomycin Content of Aqueous, Expressed in Micrograms per Cubic Centimeter After Local Administration of 0.5 Per Cent Aureomycin Borate Solution by Three Methods*

Hours after local administration...	Corneal Bath for 5 Min.		Cathode Iontophoresis at 1.6 Milliamperes for 5 Min.			Subconjunctival Injection of 0.5 cc., 2,500 Micrograms	
	½	1	½	1	2	½	1
	—	—	0.05	>0.05	>0.05	0.1	<0.1
—	—	—	0.1	>0.05	>0.05	0.1	<0.1
—	—	—	<0.1	>0.05	0.1	0.1	0.1
—	—	—	<0.1	>0.05	0.2	<0.1	>0.05
—	—	—	<0.1	0.1	0.1	<0.1	>0.05
—	—	—	<0.1	0.1	0.1	>0.05	>0.05
—	—	—	...	0.1	0.1	...	>0.05
—	—	—	...	0.1	0.1	...	....

iris and ciliary body, lens and vitreous were weighed, and ground with Berkshire sand and a phosphate buffer solution, the latter also being used to wash down the weighing bottle, mortar and pestle. The ground-up material with the washings was transferred to a centrifuge tube and diluted to approximately twenty times the weight of the given tissue. It was necessary to calculate the dilution factor for each specimen, because varying amounts of buffer were required for the washings. Purposely, the least possible amount of buffer was used so that the dilution factor might be kept as low as possible. The material was centrifuged at moderate speed for twenty minutes, and the supernatant fluid was assayed for aureomycin concentration, employing the test previously described. Between the various steps of the procedure the material was kept in the refrigerator. The heart blood was allowed to cool and clot at room temperature, and the centrifuged serum was used for the bioassay.

RESULTS

*Local Application.*—Table 1 presents the results of topical application. Since 0.05 microgram per cubic centimeter is the end point in the method of bioassay used, smaller quantities of aureomycin, if pres-

ent in the aqueous, were not detected by this test. Because of the small amounts of aqueous and the nature of the test, which required at least 0.25 cc. of solution for the 0.05 microgram per cubic centimeter concentration and another 0.25 cc. sample for subsequent higher concentrations, it was technically impossible to test for 0.05 micrograms per cubic centimeter or for higher concentrations with aqueous from the same eye. This explains the use of the < and > signs in the tables.

TABLE 2.—*Distribution of Aureomycin in Aqueous, Ocular Tissues, Serum and Spinal Fluid, Expressed in Micrograms per Cubic Centimeter of Fluid or per Gram of Solid Tissue, Following Oral Administration of 50 Mg. of Aureomycin Hydrochloride per Kilogram of Body Weight*

Hours after oral administration.....	1	2	3	4
Cornea.....	—	—	—	—
	—	—	—	—
	—	—	—	—
Sclera.....	—	—	—	—
	—	—	—	—
	—	—	—	—
Iris and ciliary body....	—	—	—	—
	—	—	—	—
	—	—	—	—
Lens.....	—	—	—	—
	..	—	..	—
Aqueous.....	—	—	—	—
	—	—	—	—
	—	—	—	—
Vitreous.....	—	—	—	—
	..	—	..	..
Blood.....	2.0	2.0	0.5	0.5
	2.0	1.0	1.0	0.5
	..	..	0.8	..
	..	..	..	..
Spinal fluid.....	—	—	—	—
	..	—	—	—

The corneal bath, while nonirritating and not causing any staining defect, did not introduce measurable quantities of aureomycin into the eye. Iontophoresis, on the other hand, secured in the aqueous amounts of aureomycin varying from 0.05 to 0.2 microgram per cubic centimeter. Fluorescein staining of the cornea after iontophoresis indicated small lesions of the epithelium of all eyes at four hours, with disappearance of the staining defect within twenty-four hours in all but 2 eyes. At forty-eight hours all eyes were clear, showing no congestion or staining defects.

Subconjunctival injection produced about the same concentration of aureomycin in the aqueous as did iontophoresis, but there was more irritation. After twenty-four hours there was severe conjunctival congestion, with some chemosis and slight conjunctival discharge. Yellowish discoloration of the conjunctiva at the site of the injection, still pronounced at four hours, disappeared at the end of twenty-four hours. At forty-eight hours there was some conjunctival congestion, but no

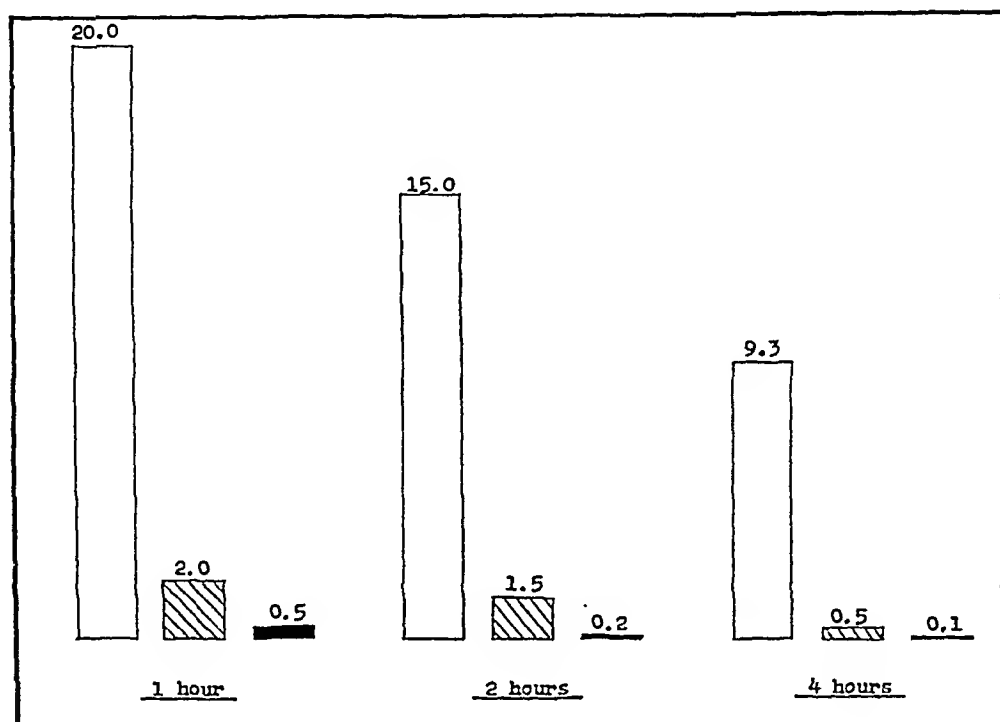
TABLE 3.—*Distribution of Aureomycin in Aqueous, Ocular Tissues, Serum and Spinal Fluid After Intramuscular Administration of 20 Mg. of Aureomycin Hydrochloride per Kilogram of Body Weight, Expressed in Micrograms per Cubic Centimeter of Fluid or per Gram of Solid Tissue*

Hours after intramuscular administration...	1	2	4
Cornea.....	—	—	—
	—	—	—
	—	—	—
Sclera.....	—	—	—
	—	—	—
	—	—	—
Iris and ciliary body.....	—	—	—
	—	—	—
	—	—	—
Lens.....	..	..	—
	..	..	—
Aqueous.....	—	—	—
	—	—	—
	—	—	—
Vitreous.....	—	—	—
	—	—	—
	—	—	—
Blood.....	0.5	0.2	0.05
	0.4	0.2	0.1
	..	..	..
	..	..	..
Spinal fluid.....	—	—	—

chemosis or conjunctival discharge. These changes were noted in all the eyes treated, with only minor differences, and were most pronounced over the site of the subconjunctival injection.

*Systemic Administration.*—The oral and intramuscular methods, as shown in tables 2 and 3, showed no detectable amounts of aureomycin in the fluids and tissues of the eye or in the spinal fluid. The blood levels were rather consistent in relation to the amount administered and the time interval before the determination. The blood levels reached by the intramuscular route of administration were higher than those obtained by the oral method (chart).

The intravenous method of administration (table 4) produced fairly constant concentrations in the aqueous, varying from 0.05 to 0.4 micrograms per cubic centimeter, the concentration depending on the time of the test. The concentrations in the other tissues of the eye were more variable, ranging from 0 to 3.84 micrograms per gram of tissue, but at no time was aureomycin detected in the lens. The levels of the drug in the spinal fluid generally were slightly lower than the concentrations in the aqueous. The concentrations in the blood were fairly uniform and were considerably higher with this method than with the oral and intramuscular methods.



Comparative blood levels of aureomycin, expressed in micrograms per cubic centimeter, following intravenous injection of 20 mg. of aureomycin hydrochloride per kilogram of body weight, intramuscular injection of 20 mg. of aureomycin hydrochloride per kilogram of body weight and oral administration of 50 mg. of aureomycin hydrochloride per kilogram of body weight.

Values for intravenous injections are represented by clear rectangles; values for intramuscular injection, by hatchures, and values for oral administration, by black areas.

#### COMMENT

Topical administration by various methods showed poor penetration of the drug into the anterior chamber of rabbit eyes. The 0.5 per cent solution was used because, according to Braley,<sup>4</sup> higher concentrations are irritating to the eye. The corneal bath gave no detectable amount of aureomycin in the aqueous. Iontophoresis and subconjunctival injection produced approximately the same aqueous levels; but, while the side effects of iontophoresis were temporary and negligible, subconjunctival injection produced considerable irritation and damage.

4. Braley, A. E.: Personal communication to the author.



Harned<sup>5</sup> found the drug highly irritating if given subcutaneously or intramuscularly. This irritating effect is somewhat overcome by combining aureomycin with procaine. When the aureomycin-procaine solution was tested against controls, its antibacterial activity was found to be the same as that of aureomycin in distilled water.

According to the principles of ionic transfer, anode rather than cathode iontophoresis should be used with aureomycin borate, since the aureomycin is present as a cation. However, anode iontophoresis

TABLE 4.—*Distribution of Aureomycin in Aqueous, Ocular Tissues, Serum and Spinal Fluid Expressed in Micrograms per Cubic Centimeter of Fluid or per Gram of Solid Tissue, After Intravenous Administration of 20 Mg. of Aureomycin Hydrochloride per Kilogram of Body Weight*

Hours after intravenous administration.....	½	1	2	4	6	8	12	18	24
Cornea.....	Trace	—	Trace	1.2	Trace	Trace	Trace	—	—
	—	—	1.5	1.4	Trace	—	—	—	—
	—	1.0	1.0	1.6	—	1.3	—	..	..
	—	1.0	1.6	1.6	—	1.3	—	..	..
	—	2.4	1.4	1.6	1.4	1.7	...	..	..
	—	2.6	1.5	2.9	1.8	1.2	...	..	..
Sclera.....	1.0	1.4	1.0	2.5	1.2	0.7	1.0	—	—
	1.2	2.0	0.6	1.7	1.2	1.5	1.3	—	—
	1.2	1.9	1.1	1.3	0.9	1.0	0.6	..	..
	1.6	2.2	1.3	1.4	0.9	1.0	1.0	..	..
	0.5	3.8	2.1	1.2	1.2	1.7	...	..	..
	0.9	2.3	2.3	2.1	1.2	1.3	...	..	..
Iris and ciliary body..	—	1.9	—	1.6	1.5	—	—	—	—
	—	2.3	—	1.4	1.4	—	—	—	—
	3.1	0.0	1.4	1.5	Trace	—	—	..	..
	3.1	1.7	1.4	1.4	Trace	—	—	..	..
	1.4	2.2	1.7	1.5	1.4	—	...	..	..
	1.1	2.9	1.3	1.5	Trace	Trace	...	..	..
Lens.....	—	—	—	—	...	...	Trace	—	—
	...	...	—	...	...	...	—	—	..
Aqueous.....	0.1	0.1	0.2	0.4	0.2	0.1	0.1	0.05	—
	0.2	0.2	0.2	0.2	0.2	0.1	0.1	0.05	—
	0.2	0.2	0.2	0.2	0.1	0.1	0.05	—	—
	0.2	0.1	0.2	0.2	0.1	0.1	0.1	—	—
	0.4	0.2	0.2	0.2	0.1	0.2	...	..	..
	0.2	0.1	0.2	0.2	0.1	0.1	...	..	..
Vitreous.....	Trace	—	—	0.1	0.1	0.05	0.05	—	—
	—	—	—	0.05	...	0.05	0.05	—	—
	...	...	0.1	—	...	Trace	—	..	..
Blood.....	30.0	20.0	10.0	10.0	8.0	5.0	2.0	0.5	0.2
	20.0	20.0	20.0	8.0	5.0	5.0	1.0	0.5	0.2
	50.0	20.0	15.0	10.0	5.0	5.0	...	..	..
Spinal fluid.....	0.0	0.2	0.2	Trace	Trace	0.1	0.05	Trace	—
	...	...	0.1	0.05	0.05	0.1	Trace	—	..
	...	...	...	0.1	0.05	...	...	..	..

with aureomycin produced such a severe reaction, marked corneal haziness and large staining defect that it was not considered safe; therefore cathode iontophoresis was used, which was relatively well tolerated. This reversal of the poles probably limits the penetration of the drug into the anterior chamber, as von Sallmann<sup>6</sup> showed in the case of penicillin iontophoresis, but was necessitated by the difficulties mentioned.

5. Harned, B. K., and others: The Pharmacology of Duomycin, Ann. New York Acad. Sc. **51**:182 (Nov.) 1948.

6. von Sallmann, L.: Controversial Points in Ocular Penicillin Therapy, Tr. Am. Ophth. Soc. **45**:570, 1947.

The question arises as to the probable antibiotic effect of aureomycin in concentrations obtained in the aqueous by local application. In vitro sensitivity tests for aureomycin against common pathogens of the eye were performed by Dornbush.<sup>7</sup> His results collaborated the findings of the present study, in which twenty-two strains of hemolytic, coagulase-positive and mannitol-positive *Staphylococcus aureus* were examined. They showed inhibition by 0.1 to 1.0 microgram of aureomycin per cubic centimeter of solution, a concentration which was about the same as that obtained by topical administration. It is known that in the case of penicillin, streptomycin and bacitracin<sup>8</sup> aqueous levels are much higher than the in vitro sensitivity end points of most strains of pathogenic *Staph. aureus*. Thus, it would appear that in the case of penicillin, streptomycin and bacitracin a considerable margin of safety exists, as expressed by the difference between the aqueous concentration of the antibiotic and its in vitro sensitivity. This margin of safety was not found to exist with aureomycin.

With the oral method of administration, 50 mg. per kilogram of body weight was chosen as the dose because it corresponds approximately to the amount given to adult human subjects (Braley<sup>4</sup> gave about 3 Gm. per twenty-four hours to the average adult of 60 Kg.). This amount showed no apparent toxic effect—no emesis or diarrhea—but gave very low blood levels and no detectable amounts in the eye. The intramuscular administration seemed painful to the animal; although it provided higher blood concentrations, it, again, did not penetrate the blood-aqueous barrier in measurable amounts. Absorption from the muscles seemed slow and inadequate, as shown by the relatively congested, edematous muscles at the site of injection after the animal was killed and dissected. This can be compared to the poor absorption of the drug from the subconjunctival injection. Both the conjunctiva and the muscle were edematous, swollen and yellowish several hours after administration of the drug. The irritating effect of the drug can be further seen with the intravenous method of administration; as long as the solution passed directly from the needle into the vein, the animal remained relatively quiet; but if small amounts of the solution leaked into the subcutaneous tissues, the animal became highly excited.

With relatively high blood levels obtained by intravenous administration, measurable concentrations of the drug were detected in various tissues. However, in all the solid tissues of the eye, zero results actually represented only the end point of the bioassay (0.05 micrograms per cubic centimeter multiplied by the dilution factor previously mentioned).

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7. Dornbush, A. C.: Personal communication to the author.

8. Locke, J. C.: Experimental Studies with Antibiotics (Bacitracin, Streptomycin, Penicillin) and Antibiotic Mixtures, in Intraocular Infections with Penicillin-Resistant *Staphylococci*, Proc. A. Research Ophth., June, 1948, to be published.

The average value for this dilution factor was 20; therefore  $20 \times 0.05 = 1.0$ , which means that actually concentrations less than 1.0 microgram per cubic centimeter were not detected with this test. This factor varied somewhat, being sometimes as low as 10 and sometimes as high as 30, depending on the least amount of buffer necessary for washing down the ground-up material. Therefore in a few instances results less than 1.0 microgram per gram were obtained.

An interesting feature was the slow rate of disappearance of the drug from the various ocular tissues. Six to eight hours after intravenous injection the concentrations were only slightly less than one or two hours after the injection, and the disappearance curve was flat. This observation was contrary to the results for other antibiotics when administered intravenously.

To rule out the possibility that aqueous inhibits the antibacterial activity of aureomycin, a series of experiments was carried out on normal rabbit aqueous. Aureomycin borate was diluted with broth to contain 2.0 to 0.2 microgram per cubic centimeter in different concentrations; the aureomycin solution was mixed with normal aqueous and then assayed, the conditions thus simulating those present in vivo. No inhibitory action was found.

The results reported in the present series of experiments indicate limitations of the applicability of aureomycin because of its irritating property and its slow absorption by the tissues. Another disadvantage is the rapid inactivation of the drug when kept in solution. It must be remembered, however, that the development of this antibiotic is in an early stage and that these disadvantages may be remedied in the near future.

#### SUMMARY AND CONCLUSION

Experiments were carried out to ascertain the penetrability of aureomycin into the normal rabbit eye, with the following results:

1. After corneal bath no aureomycin was detected in the aqueous.
2. Iontophoresis and subconjunctival injection produced low levels in the aqueous. Iontophoresis was fairly well tolerated by the eye, but subconjunctival injection was irritating to such an extent that it was considered contraindicated.
3. Aureomycin did not penetrate into the eye when given orally or intramuscularly, although blood levels were obtained with both methods.
4. The cornea, sclera, iris and ciliary body, aqueous, vitreous and spinal fluid showed appreciable concentrations of aureomycin when large amounts were given intravenously.

As compared with other antibiotics, aureomycin is more irritating and penetrates less readily into the eye; but once it has crossed the blood-aqueous barrier, it remains longer in the ocular fluids and tissues.

## USE OF TANTALUM FOR OCULAR DRAINAGE

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THE PURPOSE of the present study was to review past efforts designed to lower the intraocular tension by various types of seton operations and to devise new technics using laboratory animals and suitable human subjects. While the implantation of foreign materials into the eye for the treatment of glaucoma has not been well accepted, either in principle or in ophthalmic practice, the literature contains several enthusiastic reports of this type of procedure.

### HISTORICAL REVIEW

In 1906 Rollet and Moreau<sup>1</sup> reported 18 cases in which they treated hypopyon associated with corneal ulcer by a double paracentesis of the lower portion of the cornea, through which punctures a horsehair was threaded. Either end of this seton was glued to the cheek with collodion, and the thread was left in situ for forty-eight hours. The next year Rollet<sup>2</sup> applied this procedure to the treatment of 2 patients with painful absolute glaucoma with satisfactory results. He suggested that such a technic might be useful in the treatment of inflammatory glaucoma.

In 1912 two Englishmen, Zorab and Mayou,<sup>3</sup> working independently, in the same issue of the *Ophthalmoscope* reported on methods of draining the anterior chamber by a permanent silk thread implant, the thread acting as a wick that drained under the conjunctiva. Mayou used a 5 mm. length of single thread knotted at one end which he introduced just anterior to the root of the iris in the lower temporal quadrant. He reported on the results of this treatment in 4 cases of glaucoma and, a year later, in an additional 10 cases.<sup>4</sup> In 11 of the

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1. Rollet, M., and Moreau, M.: *Rev. gen. d'ophth.* 25:481, 1906.

2. Rollet, M.: *Rev. gen. d'ophth.* 26:289, 1907.

3. Zorab, A.: *Ophthalmoscope* 10:259, 1912. Mayou, M. S.: *ibid.* 10:254, 1912.

4. Zorab, A.: *Ophthalmoscope* 11:211, 1913.

14 cases the tension was controlled successfully. Zorab described two procedures; the first consisted in passing a silk suture under the conjunctiva through the corneoscleral junction, across the anterior chamber and out through the limbus on the other side under the conjunctiva. This produced a double subconjunctival wick, but the difficulty of passing the suture made him abandon this procedure in favor of a second procedure, described as "aqueoplasty." Aqueoplasty consists in inserting a double silk loop through a small superior keratome incision 2 mm. behind the limbus and burying it under a conjunctival flap. He reported 23 cases of glaucoma in which he used these technics. In 18 cases the tension was controlled; in 4 cases the silk was not retained, and in 1 case the tension was not controlled.

Three years later (1915) Wood<sup>5</sup> described 3 cases of absolute glaucoma in which he used the Zorab aqueoplasty technic to control the tension and pain. He was so impressed with the success in these cases and in those reported in the literature that he devised his own technic, using a Graefe knife with a hole in the distal end of the blade. After the knife had been used to transfix the sclera at about 11 and 1 o'clock just behind the corneoscleral junction, the hole was threaded and the knife was withdrawn. The suture was cut, leaving a double strand across the anterior chamber. The free ends were threaded on needles, and then they were carried in a fanlike manner under the conjunctiva, where they were buried. He presented 2 cases in which this method was successful.

Vail<sup>6</sup> (1915) described a case of absolute glaucoma which he treated by drainage of the vitreous. He used a no. 10 plaited black silk ligature, which was carried on a heavy needle through all the coats of the eye in the region of the ora serrata and carried back and out through the same layers. Each end of the suture was buried under Tenon's capsule, the thread resting on the episclera as far back as the equator. Vail reasoned that Tenon's space was better equipped to handle drainage than the subconjunctival space.

The Vail operation is of interest because of the later report of Weekers<sup>7</sup> (1922), who described a new principle in the treatment of glaucoma. Weekers expressed the belief that from the standpoint of where the damage is done, all glaucoma is essentially hypertension of the posterior segment. He stated that permanent decompression of the posterior segment is essential, and he proposed and used a little hollow gold cuff, 2 mm. wide and 1.5 mm. in height, to rest in a scleral trephine hole 7 mm. back from the limbus, buried under the conjunctiva and Tenon's capsule. He expressed the opinion that the

5. Wood, C. A.: *Ophth. Rec.* **24**:179 and 235, 1915.

6. Vail, D. T.: *Ophth. Rec.* **24**:184, 1915.

7. Weekers, L.: *Arch. d'ophth.* **39**:279, 1922.

gold implant was essential to prevent the scleral wound from closing, since his microscopic studies showed that posterior sclerectomies became closed over. He mentioned that the operation was performed in several cases of absolute glaucoma with good results and that gold was well tolerated by the eye.

The tolerance of the eye for gold was substantiated by Stefansson<sup>8</sup> (1925), who reported its use in the form of a T-shaped insert in a keratome incision at 12 o'clock. The vertical portion of the T extended into the chamber, while the two limbs rested on the sclera, buried under the conjunctiva. In some cases a twisted gold wire was used; in others, a hollow tube, and in some, a solid gold implant with a spiral vertical portion. The chief complication seen was the puncture of the conjunctiva by the gold wire, in 2 of the early cases. The implant became dislocated in 1 case, and atrophy of the iris was observed in a few cases in which the gold came in contact with the iris. In the average case the follow-up period was three years, although in some the period of observation was only a few weeks. A total of 32 eyes were treated by this method, and the pressure was controlled in 80 per cent.

The first to use implants in the suprachoroida was Row<sup>9</sup> (1934), who performed cyclodialysis and introduced a platinum-iridium wire experimentally into the cleft. The procedure was too traumatic and a cataract developed. Horsehair proved to be more satisfactory but had to be introduced with a grooved director as a guide. In 3 cases of glaucoma in man the condition was controlled with cyclodialysis and horsehair implants. Row emphasized the importance of burying the ends of the horsehair under Tenon's capsule to avoid having the stiff end work its way out through the conjunctiva.

A modification of the old Zorab operation was described as recently as 1936 by Wolfe and Blaess.<sup>10</sup> At 5 and 7 o'clock small conjunctival flaps were turned down, and two small keratome incisions were made into the chamber at the limbus. A lacrimal needle was employed to carry the thread across the chamber through the keratome incisions. The authors reported 6 cases in which this treatment was successful. They mentioned the value of subconjunctival manipulation of the suture in the event of a later rise of tension.

Troncoso<sup>11</sup> (1940) ingeniously proposed magnesium to be used as an implant after cyclodialysis. The magnesium was introduced into

8. Stefansson, J.: *Am. J. Ophth.* **8**:681, 1925.

9. Row, H.: Operation to Control Glaucoma: Preliminary Report, *Arch. Ophth.* **12**:325-329 (Sept.) 1934.

10. Wolfe, O. R., and Blaess, M. J.: *Am. J. Ophth.* **19**:400, 1936.

11. Uribe Troncoso, M.: Cyclodialysis with Insertion of a Metal Implant in the Treatment of Glaucoma: A Preliminary Report, *Arch. Ophth.* **23**:270 (Feb.) 1940.

the cleft and by the end of two weeks the metal had disappeared. The rapid oxidation was attended with a moderate inflammatory reaction and the production of hydrogen bubbles and ultimately by pockets of fibrosis in the cyclodialysis tunnel. A thin but dense fibrous capsule formed around gas bubbles trapped in the suprachoroida. In no eye examined could a continuous channel be demonstrated. There were proliferative changes in the pigment epithelium, scattering of pigment and small round cell infiltration. Troncoso reported on 10 human eyes, 7 of which had had previous operations. There were good results in 2 eyes, apparently good results in 4 and poor results in 4.

#### EXPERIMENTAL STUDY

A review of the literature has shown that a subconjunctival implant at the limbus is poorly supported and easily displaced and that it tends to erode through the conjunctiva. This was confirmed in preliminary experiments in rabbits, and for this reason attention was directed to suprachoroidal drainage.

Cyclodialysis is one of the accepted methods in the treatment of glaucoma. It is effective only so long as the chamber angle remains open. When the cleft closes, the tension rises. If one could prevent the reattachment of the ciliary body after cyclodialysis, one should be able to maintain suprachoroidal drainage. To prevent this reattachment, a wedge of physiologically acceptable material placed in the cyclodialysis cleft should provide drainage. Tantalum, according to Burke,<sup>12</sup> is the most inert metal known, having a half-life of 955 years in concentrated sulfuric acid at 147 C. The lack of reactivity is due to the fact that a tenacious oxide film forms on its surface, preventing the transfer of electrons to the tissues. Studies of the tolerance of extraocular tissues to this substance indicate that a single layer of fibroblasts forms around a tantalum implant with no inflammatory response. A study of the ocular reactions to tantalum was therefore undertaken.

*Reaction of the Eye to Tantalum.*—The first study was concerned with the reaction of the eye to a piece of tantalum wire inserted into the anterior chamber. Under sterile precautions, a 4 mm. length of tantalum wire was inserted into the anterior chamber of albino rabbits by loading a 22 gage, 1½ inch (3.8 cm.) needle. The cornea was pierced with the needle, and the tantalum wire was pushed into the chamber by means of a stylet.

The reactions of 12 rabbit eyes were studied, and eyes were removed serially at one, three, five and eight days. Four eyes were observed

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12. Burke, G. L.: Corrosion of Metals in Tissues; an Introduction to Tantalum, *Canad. M. J.* **43**:125-128, 1940.

for two and one-half months and 2 for six months. Except for slight infiltration at the site of paracentesis, the corneal reaction was nil. For a day or two after the paracentesis the vessels of the iris showed some dilatation, which subsided by the third day. In some eyes a small amount of fibrin formed around the implant where it adhered to the iris; this disappeared in a few days, and the tantalum fell into the chamber angle below.

The microscopic reaction to the tantalum was studied in two ways. It was felt desirable to study the reaction with the metal *in situ*. The eyes were fixed in dilute solution of formaldehyde U. S. P. (1:4) for twenty-four hours, and then the iris was dissected out and washed in distilled water, care being taken to prevent the tantalum from becoming dislodged. The anterior surface was then painted with hematoxylin by means of a camel's hair brush to stain the endothelial cells and the cells of the anterior stroma. The irides were then cleared in the routine manner and mounted in full thickness for study.

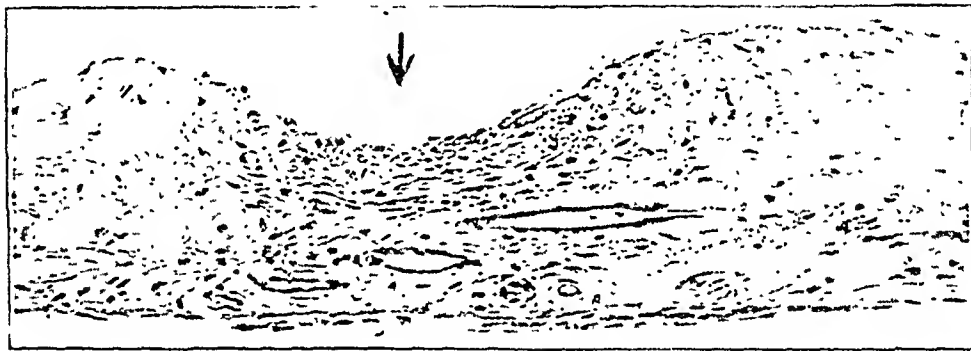


Fig. 1.—Tantalum wire had been in contact with the iris for a week (arrow). A few mononuclear cells are present, but no inflammation. The endothelial surface of the iris appears intact.

At the same time, routine meridionally cut sections were made after fixation in Zenker's solution. To prepare these sections it was necessary to remove the metal before sectioning, but the eyes were cut through the area from which the tantalum had been removed.

Microscopic study indicated that there was no inflammatory response at the site of contact between the uvea and the tantalum. A small amount of fibrin formed on the surface of the tantalum. This was attributed to the high fibrin content of the rabbit's secondary aqueous rather than to any reaction evoked by the tantalum. In no section was any inflammatory reaction observed (fig. 1).

The tissue acceptability of tantalum was also demonstrated by implanting 26 gage wire into the midstroma of the cornea. The implantation was accomplished by loading a 3 mm. length of wire into a 22 gage needle, which was inserted into the midstroma of the



cornea. The wire was ejected into the stroma by a stylet. Tantalum was compared with silver, a copper alloy and with stainless steel. The results are summarized in figure 2, which shows that tantalum remained longer than any of the other materials tested. There was no inflam-

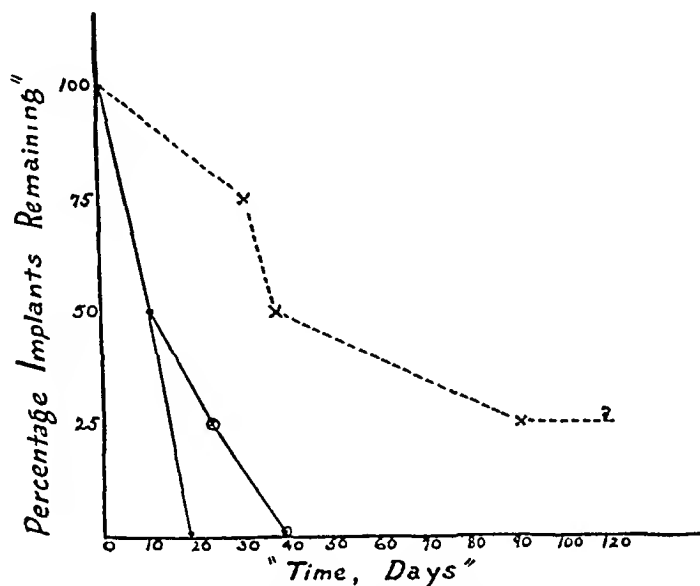


Fig. 2.—Tissue acceptability of various types of intralamellar corneal implants. Values for tantalum are shown by the broken line; values for silver and a copper alloy, by the line with solid dots, and values for stainless steel, by the line with hollow circles.

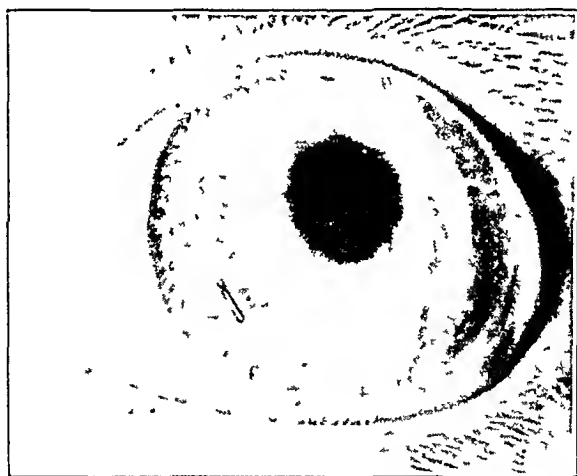


Fig. 3.—A small piece of tantalum wire implanted in the corneal stroma showed no reaction at the end of four weeks.

matory reaction in the cornea around the tantalum, whereas the other materials produced varying degrees of inflammation (fig. 3). One tantalum implant remained for four months, at which time the animal was used for another experiment.

*Use of Tantalum Wire.*—A series of preliminary operative procedures was undertaken in which braided tantalum wire loop was used in several ways. In 2 albino rabbits it was used as an inclusion in a keratome incision into the anterior chamber. The ends of the wire were buried under a conjunctival flap. In 2 other animals it was placed in contact with the anterior surface of the lens through a keratome incision made directly through the ciliary body. The ends were buried under the conjunctiva. In another 2 rabbits the tantalum wire was used as an implant in the suprachoroidea. It was observed that tantalum was well tolerated at these sites, that the operative wounds healed well and that the eyes remained quiet for four months without inflammatory or degenerative changes. It was noted that the tantalum wire cut through the conjunctiva when it was buried near the limbus. The tantalum wire in all operative sites was incorporated in the scar and seemed to form an integral part of the wound. Fibroblasts grew into the meshwork of the braided tantalum. India ink was injected into the anterior chamber of these eyes. In 2 animals with the keratome incisions near the limbus a small amount of ink could be observed under the conjunctiva near the wound. In the other animals the ink was difficult to trace and none appeared to pass through the scleral wounds, although it followed the path of the tantalum wire as far as the sclera. It was concluded that tantalum wire could be of no assistance in the development of a fistula, since the fibroblasts grew into the interstices of the wire, incorporating it into the tissues.

*Use of Tantalum Plates.*—Special cyclodialysis implants were prepared by Mr. A. Goebels, of the Wilmer Ophthalmological Institute. These implants were 2 mm. wide and 9 mm. long and were bent on a radius of curvature of 7 mm., which corresponds closely to that of the curvature of the rabbit's sclera. The edges were carefully rounded, and the implants were polished with jeweler's rouge. The posterior 2 mm. of the implant was bent at about a 120 degree angle with the main portion of the implant. This provided a small lip, which was held firmly by a mosquito clamp in inserting the plate into the cyclodialysis cleft. This lip projected out through the sclerectomy wound and could be seen through the conjunctiva after the flap had been sutured. In the rabbit it was necessary to start the cyclodialysis well back, almost at the equator, about 8 mm. from the limbus, to prevent getting into the ciliary sinus instead of the suprachoroidea. It was found necessary to use a sharpened cyclodialysis spatula to cut through the firm attachment of the ciliary body to the sclera. With this sharpened instrument, care was exerted not to injure Descemet's membrane. At the termination of the procedure, the end of the implant

could be seen in the angle by placing a little pressure on the sclera above the implant. Hemorrhage was avoided by keeping away from the long ciliary vessels.

Eight operations with tantalum implantations were performed. Four cyclodialyses without tantalum implantations were done as controls. In 4 of the 8 eyes, the implants were removed at the end of four weeks. It was noted at the time of removal that there was a free flow of aqueous on the incision of the conjunctiva overlying the posterior



Fig. 4.—The suprachoroidal endothelium-lined cleft between the iris and ciliary body, below, and the corneoscleral junction and sclera, above, provided a free channel of drainage from the anterior chamber to the episcleral tissues. The tantalum had been in place two months and had been removed just prior to fixation.

lip of the implant. There was no apparent scarring of the subconjunctival or episcleral tissues, and the implants slipped out with ease. A month later gonioscopy revealed the cleft to be wide open in 1 eye, to be partially closed over in 2 eyes and to be completely closed in the fourth eye. The cyclodialysis clefts of the 4 control eyes were completely closed by the second week. In the other 4 eyes, the

tantalum implants were permitted to remain for a total of eight weeks. In these eyes, 0.1 cc. of a 2 per cent solution of fluorescein sodium in a tuberculin syringe was mixed with the aqueous through an oblique puncture wound in the cornea. No pressure was exerted, and the syringe, containing 0.1 cc. of the aqueous-fluorescein mixture, was withdrawn. In a few moments one could observe the fluorescein subconjunctivally about the sclerotomy end of the tantalum implant. On incision of the overlying conjunctiva, a free flow of greenish fluid was observed. These eyes were removed for histologic examination. A

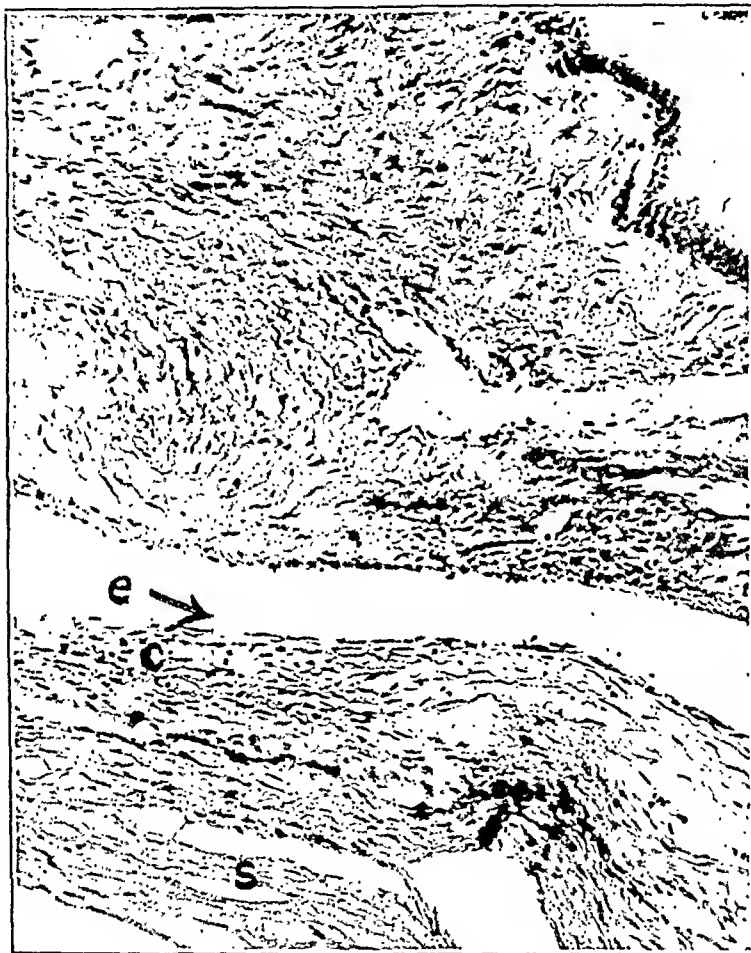


Fig. 5.—The midportion of the channel between the ciliary body and the sclera shows a loose network of connective tissue (*c*) between the endothelial lining (*e*) and the sclera (*s*).

small pannus was observed in 3 of the 8 rabbit eyes in the region of the implant.

It was concluded that tantalum acted as a physiologically acceptable wedge between the ciliary body and the sclera and that the aqueous could filter around the implant and out the sclerotomy wound to the episcleral tissues.

*Pathologic Studies.*—Microscopic examination of the 4 eyes that carried implants for two months showed plainly that a continuous cleft

ran from the chamber to the episclera (figs. 4, 5 and 6). The tantalum became lined with a layer of flat cells, which were indistinguishable from the endothelial cells on the anterior surface of the iris. On the scleral, as well as on the ciliary, side of the cleft, underlying this endothelial lining was an area of loosely organized connective tissue. From the anterior edge of the sclerotomy wound a rather dense mass of episcleral connective tissue appeared to be growing downward and forward into the suprachoroidea. This connective tissue, as well as the posterior lip of the sclerotomy wound, was covered with the same layer of endothelial cells as that which lined the rest of the cleft.

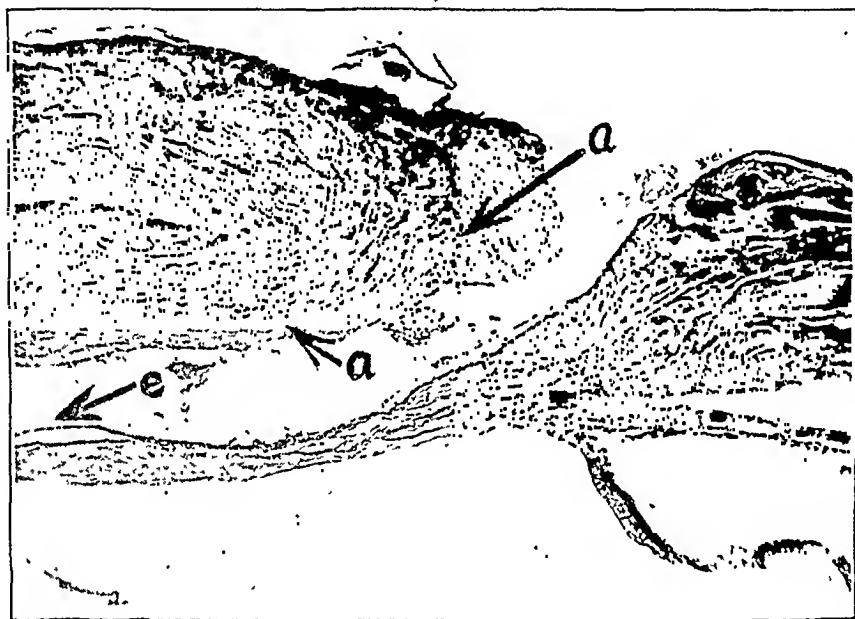


Fig. 6.—At the posterior end of the channel from the anterior chamber to the episcleral region, a downgrowth of episcleral fibrous tissue (*a*) turning forward into the cyclodialysis tunnel is observed. The tantalum plate was removed prior to fixation. The endothelial lining (*e*) is well seen.

#### TANTALUM IMPLANTS IN HUMAN SUBJECTS

On the basis of the microscopic observations, which showed absence of inflammatory reaction and a thin layer of endothelial cells lining the cyclodialysis cleft, it was considered justifiable in certain desperate cases to undertake the treatment of glaucoma with tantalum implants. In view of the downgrowth of episcleral fibrous tissue into the cyclodialysis tunnel in the rabbit, it was considered wise to modify the procedure of tantalum implantation for the human eye.

In order to avoid episcleral tissue downgrowth, it was decided to bury the tantalum plate in the suprachoroidea. For this purpose, implants 2 mm. wide, 0.25 mm. thick and 8 mm. long, bent on a radius

of curvature of 11 mm., were prepared. They were highly polished, with rounded edges. One millimeter from one end a 0.25 mm. hole was drilled, and a 00000 braided nylon suture was passed through this hole. The suture was secured by means of a square knot. One end of the suture was threaded on a small needle with a curved cutting edge. After cyclodialysis had been performed in the routine manner, the tantalum plate was inserted into the cleft by means of a curved smooth forceps. The braided nylon suture on the needle was employed to anchor the plate in the suprachoroidea. This was accomplished by passing the needle backward toward the equator of the eye in the suprachoroidal space for 2 mm. and out through the sclera, where it was tied to the other end of the suture. The suture was adjusted in such a manner that the exact position of the implant could be controlled. In each case the implant was placed so that the anterior end was visible at the limbus.

Five such operations were performed on 4 eyes. The first two operations were for congenital glaucoma; the third was for secondary glaucoma, and the last 2 operations were performed on a narrow angle type of absolute glaucoma.

#### REPORT OF CASES

CASE 1.—C. W., a 1 month old boy with congenital glaucoma, had corneas which were enlarged and extremely hazy. Tension measured 30 mm. of mercury (Schiotz) in each eye. A goniotomy was performed on the left eye. The intraocular pressure one week later was unchanged; so a cyclodialysis with tantalum implantation was performed. A week later the tension was 35 mm., and the implant was removed.

CASE 2.—J. E. C., a 6 month old girl, had congenital glaucoma, with an intraocular tension of 35 mm. (Schiotz) in the right eye and 55 mm. in the left eye. A cyclodialysis with tantalum implantation was performed on the left eye. One week later, the tension measured 5 mm., the cleft as seen gonioscopically was open and the cornea had cleared. The patient was sent home, and the tension remained controlled for three weeks, when it again became elevated. The implant was removed.

CASE 3.—T. S., a 12 year old Negro girl, had had secondary glaucoma of the left eye for five months. She had had a congenital cataract, which was treated by discission and lavage at the age of 1 year. Three years later a discission of thickened capsule was performed. Five months before her present admission two cyclodialyses had been performed on the left eye. After the second procedure tension was controlled for five months. On her admission the eye was stony hard and vision was reduced to counting fingers. A cyclodialysis with tantalum implantation was performed. The pressure rose during the third week, and the tantalum implant was removed.

CASE 4.—D. E. G., a 70 year old woman, was admitted with bilateral acute congestive glaucoma of one week's duration. There was no light perception in either eye. Tension measured 90 mm. (Schiotz) in the right eye and 68 mm. in the left eye. She was given a course of furfuryl trimethylammonium iodide

(furmethide®) and the tension fell in the left eye to 34 mm. (Schiotz). The patient refused enucleation; so iridencleisis was performed on the right eye and a tantalum implantation was performed on the left eye (fig. 7). The tension remained controlled for twelve days in the left eye, and the implant was removed. The tension then rose to 60 mm. The implant was replaced, but the tension did not fall below 40 mm. (Schiotz). Gonioscopy one week after operation revealed the tantalum plate in the angle with a small mass of fibrin about it. There was no cyclodialysis cleft except at the point of emergence of the tantalum plate. The patient was followed for a year and one-half. A small pannus developed in the cornea adjacent to the implant. At the time of this report, the chamber was still fairly shallow, and the patient complained of ciliary pain on rubbing her eye. The eye remained white, and the braided suture, which could be observed readily, had caused no irritation under the conjunctiva.

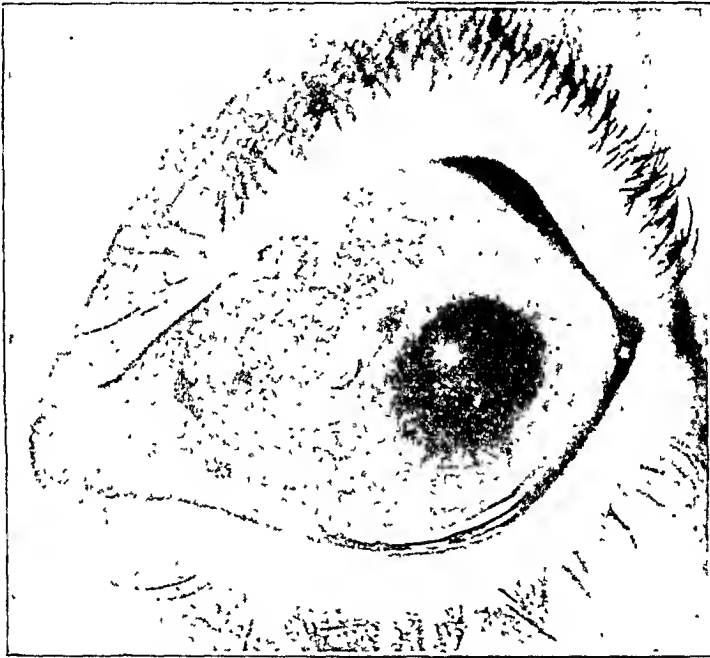


Fig. 7 (case 4).—Five days after the first operation, the tension was controlled. The implant was placed in the upper nasal quadrant.

Since in no case was the tension controlled for more than two weeks, it was concluded that mere separation of the ciliary body from the scleral spur did not constitute a functioning cyclodialysis opening. Failure in these cases was attributed to the prevention of effective suprachoroidal drainage by organization of an endothelium-lined tract about the implant. In the rabbit it had been noted that fluorescein drained about the implant when the implant came out through the sclerotomy wound. It was felt that failure in use of the implant in the human eye may have been due to the closure of the sclerotomy wound. The sclerotomy wound was closed in all instances when the second operation was performed for the removal of the implant. The use of an external fistulizing device seemed essential; for this reason, the investigation of various types of tubes was undertaken.

## . USE OF INTRAOCULAR TUBES

Stefansson was the first to report the use of intraocular tubes. His tubes were fashioned of gold, in the shape of a T and were implanted in a keratome incision in the superior part of the limbus. He found that the tension was controlled by using this device but that dislocation might occur. In order to get effective support from the tissues, and to avoid the limbal area, it was decided to use a tube running from the chamber angle through the suprachoroidal space to the episcleral tissues.

The first tubes to be employed were 24 gage platinum-iridium cannulas, made by cutting dental needles into 10 mm. lengths and bending them on a radius of curvature of 7 mm. The ends were smoothed and polished. Two such tubes were implanted in rabbits in cyclodialysis tunnels. The episcleral end projected backward



Fig. 8.—A platinum-iridium tube placed in the suprachoroidea had slipped into the anterior chamber. The photograph shows no reaction after the tube had lain in the chamber six months.

about 2 mm. beyond the sclerotomy wound, which was covered over with conjunctiva. At the end of the procedure the tube seemed firmly supported by the tissues, but after two weeks the tubes slipped into the chamber, where they remained for six months without causing any undue reaction (fig. 8). There was slight atrophy of the iris where the iris rubbed against the ends of the tubes. It was concluded that tubes had to be fixed in some way to prevent their shifting position.

When tantalum tubing became available, Mr. A. Goebbels, of the Wilmer Institute, prepared flattened tantalum cannulas for intraocular implantation in rabbits. These tubes were 9 mm. long, 2.5 mm. wide and 0.9 mm. thick, with an oval cannula 0.5 by 2.1 mm. They were bent on a radius of curvature of 7 mm. All edges were rounded and highly polished. The last 2 mm. of the convex side of the tube was removed, so that a hole 0.25 mm. in diameter could be drilled through



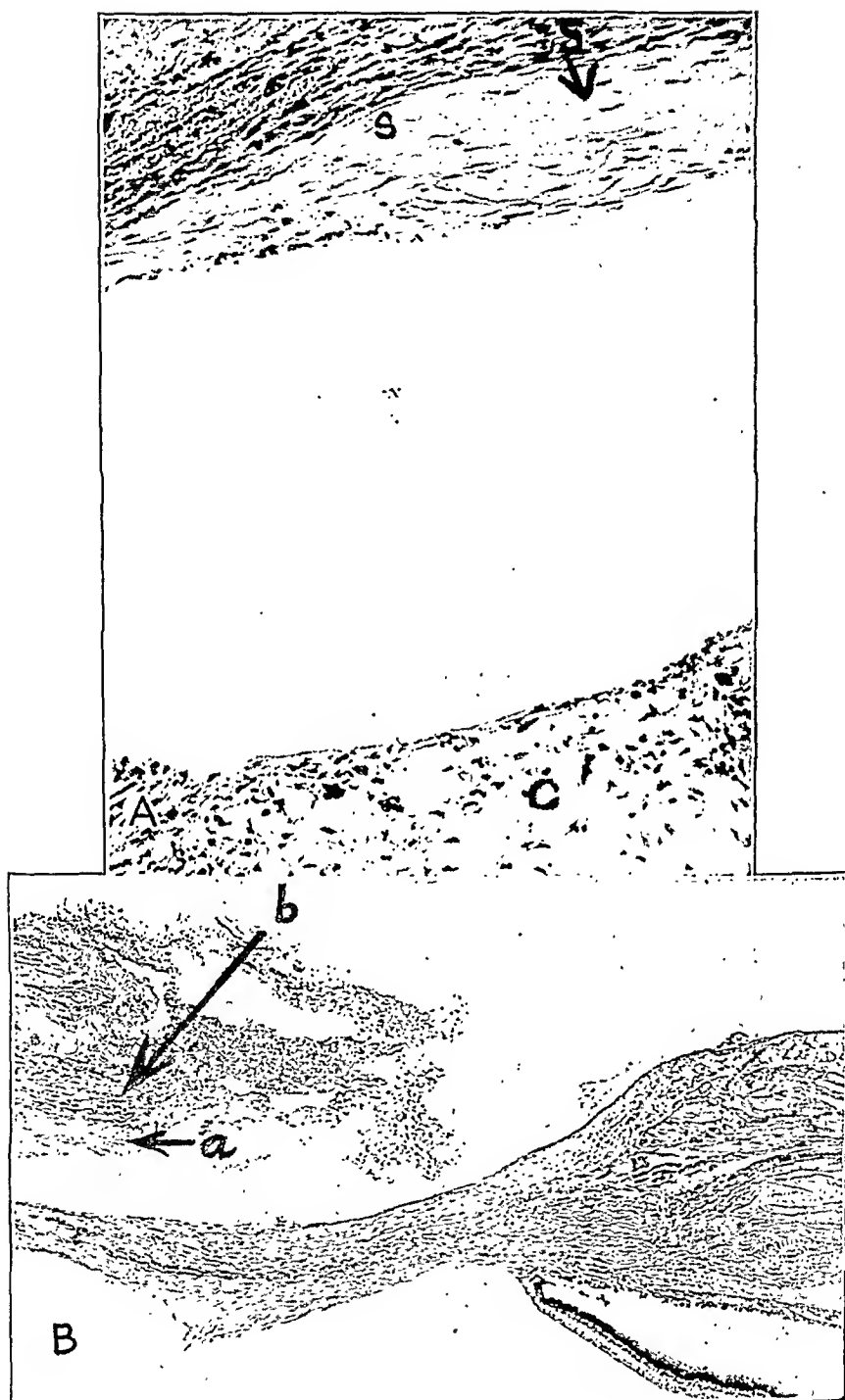


Fig. 9.—*A*, channel between the sclera (*s*) and the ciliary body (*c*) following removal of a tantalum tube.

*B*, posterior portion of a cleft following removal of a tantalum tube that had been in place nine months. This cleft is lined with endothelium. (*a*) A slight amount of fibrosis underlies the sclera; (*b*) there is no appreciable fibroblastic downgrowth from the episclera into the cyclodialysis tunnel.

the concave surface only. This edge was designed to rest on the sclera, where it was sutured with 00000 braided nylon.

Four such tubes were implanted in rabbit eyes in cyclodialysis tunnels and sutured to the sclera 2 mm. behind the sclerotomy wound. The anterior ends of the flattened tubes were permitted to project just beyond the limbus in 2 of the eyes so that they could be observed. The rabbits were followed for six months. In all 4 eyes a permanent corneal opacity developed at the limbus in the region of the implant. The further the tube projected, the larger was the opacity. A slight amount of episcleral injection persisted over the implant, but other than that the eyes showed no undue reaction and the media remained clear. Two animals were lost at the end of six months.

Nine months after implantation the remaining 2 eyes were studied as follows: A traction suture was taken in the sclera near the limbus and the eye rotated down so that the episcleral end of the tube could

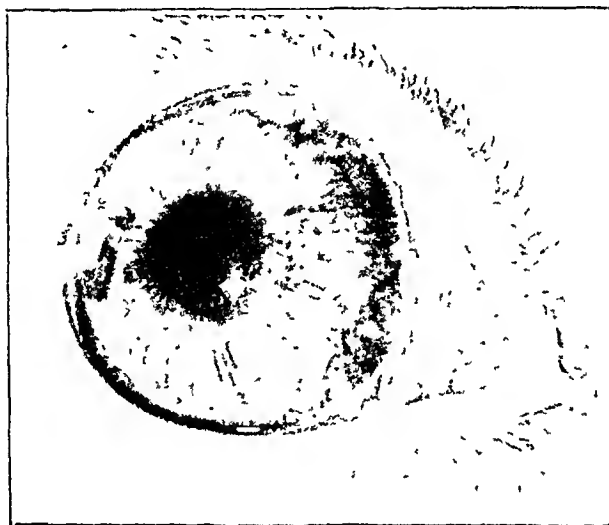


Fig. 10.—The eye one month after implantation of a tantalum tube shows a slight reaction and the presence of a permanent corneal opacity in the region overlying the anterior end of the tube.

be observed through the intact conjunctiva. One-tenth cubic centimeter of a 1 per cent solution of trypan blue in a tuberculin syringe was mixed with the rabbit aqueous through a 25 gage needle, which had been plunged obliquely through the limbus. The syringe was withdrawn with 0.1 cc. of a mixture of aqueous and trypan blue.

It was observed in both rabbit eyes that the trypan blue discolored the episcleral tissues about the posterior end of the tube in a few minutes. The eyes were enucleated, the corneas were removed and a 27 gage hypodermic needle was inserted into the end of the tube. Trypan blue was injected, and there was further discoloration in the area about the implant. The nylon sutures holding the tubes in place were cut, but episcleral scar tissue had grown through the hole about the braided nylon suture and had to be divided to remove the implant. The episcleral end of the cannulas were free from tissue, and no

tissue had grown down into the tubes. The tubes slipped out with ease. The histologic picture was essentially the same as that observed with tantalum plates (fig. 9 *A* and *B*). There had been some down-growth of episcleral tissue into the cyclodialysis tunnel, but this was not extensive.

It was concluded that, while there was no undue reaction, the development of corneal opacities and pannus in the region of the tubes was undesirable (fig. 10).

Even though tantalum is well tolerated by the tissues, the presence of some episcleral injection indicates that irritation is present. Since tantalum is inert, it is logical to conclude that the reaction must be due to the presence of a large, unyielding foreign body and that the irritation is of mechanical origin. The complaint of ciliary pain in 1 patient with a tantalum implant substantiated this observation.

#### SUMMARY AND CONCLUSIONS

The reactions of the ocular tissues to tantalum were studied. It was found that tantalum was well tolerated by the cornea, iris, ciliary body and sclera.

Endothelium-lined fistulas formed around tantalum plates inserted into cyclodialysis clefts. The channel ran from the chamber angle through the suprachoroidea and out onto the sclera. Episcleral fibrous tissue grew forward into the cyclodialysis tunnel for a short distance but did not interfere with drainage.

Four human eyes with glaucoma were treated with tantalum plates inserted into cyclodialysis tunnels. The tension was controlled for only two weeks. At the time of this report a tantalum plate has remained in an eye with absolute glaucoma for a year and a half. The tension remains at about 40 mm. of mercury (Schjøtz). The patient complains of ciliary tenderness under the implant. A small pannus has formed in the vicinity of the implant, but the eye has remained white and the media clear.

Experimental work on rabbits indicates that drainage of aqueous in the normal eye can be maintained by implanting a tantalum tube in the suprachoroidal space to extend from the chamber angle to the episcleral tissues. Local formation of pannus and injection of the episcleral vessels in these animals probably result from mechanical irritation by a rigid foreign body, which, though chemically inert, is too unyielding.

Further experimentation with similar devices should be more rewarding if a more flexible material capable of maintaining a lumen were used. Nylon tubing should be available shortly for study.

The use of a tantalum tube is justifiable as a temporary measure in desperate cases of glaucoma.

# CORNEAL TRANSPLANTATION IN CASES OF APHAKIA AND ECTOPIA OF THE LENS

Selection of Cases; Technic of Operations Outlined; Report of New Instruments

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THE PURPOSE of this article is to discuss the problem of corneal transplantation in cases of aphakia and displacement of the lens and to present a new technic and instruments for carrying out this type of operation in such cases.

Corneal transplantation has long been recognized as a highly successful procedure in properly selected cases; but there have been definite contraindications to this operation, and until recently the condition of aphakia has been considered unfavorable for operation (Rycroft and Somerset,<sup>1</sup> McArevey,<sup>2</sup> Filatov,<sup>3</sup> Elschmig,<sup>4</sup> Castroviejo<sup>5</sup>).

## APHAKIA

It is now known that corneal grafts heal and remain transparent in aphakic eyes. Cases of aphakia are by no means the most favorable, but, owing to improved technics, a reasonably good chance of a successful corneal transplantation is offered in these cases.

In cases in which both corneal leukoma and cataract are present and it has been determined beforehand that the cataract exists, it is a much simpler and safer procedure to carry out the corneal transplantation first and the cataract extraction later, after a clear central area of cornea has been obtained. The operations when done in this order are the most satisfactory, and then only does the corneal transplantation procedure present no immediate problems. I have performed a number of such operations without the occurrence of unusual complications. These results agree with the experience of Castroviejo,<sup>6</sup>

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From the Department of Surgery, Division of Ophthalmology, Western Reserve University School of Medicine and the University Hospitals of Cleveland.

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Elschnig and Filatov. However, in such cases, after the corneal transplantation has been successfully performed, there should be a considerable delay before removal of the cataract. At least six months should separate the two procedures to insure that complete healing has taken place. A cornea that reveals the diffuse scarring of interstitial keratitis, even though it has been quiescent for many years, may show reactivation of the keratitis after the extensive surgical intervention that is required when removing an area for transplantation.

This reactivation may reveal a typical picture of interstitial keratitis and be followed by complete opacification and a varying degree of vascular infiltration. Figure 1 shows such a case. The patient, a

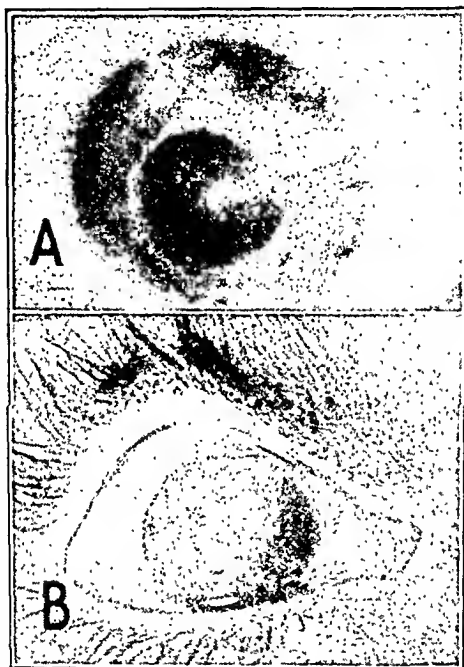


Fig. 1.—*A*, postoperative clear corneal graft; *B*, eye shown in *A* after active keratitis, resulting in opacity of graft.

woman aged 48, had old interstitial keratitis due to congenital syphilis. This had apparently been quiescent for many years. A corneal transplantation was done, and a clear graft was obtained (fig. 1 *A*). Three months after the operation, and before the cataract operation could be carried out, very active interstitial keratitis developed in this eye, which was followed by opacification of the graft with vascular infiltration and secondary glaucoma (fig. 1 *B*). This keratitis was presumably due to the trauma of the corneal transplantation, as the other eye remained quiescent throughout.

However, when the surgical procedures are carried out in the reverse order, or the cataract is removed first, the operation will progress without complications until the anterior chamber has been opened, and

then there may be an overwhelming loss of vitreous. This fact has been recognized for many years and has been reported in writing by Rycroft and Somerset, McArevey, Filatov and Elschmig. If the lens has previously been removed, there must be something in its place to keep the posterior segment intact, or as nearly intact as possible. This was early recognized by Filatov, who devised a spatula for insertion into the anterior chamber to hold back the vitreous. Theoretically, the condensation of the anterior surface of the vitreous body, commonly known as the hyaloid membrane, may keep the vitreous body intact, but the manipulation necessary in cutting the graft makes the presentation of vitreous into the anterior chamber very likely. If the cataract operation has been carried out by the extracapsular method, and the posterior capsule is intact, this membrane, of course, will act as a suitable barrier to the vitreous. When the cataract has been removed by the intracapsular method, the presence of vitreous in the anterior chamber, either as a herniation or as loose vitreous strands, is very common. Without adequate protection to the vitreous present in the anterior chamber, the maneuver of cutting the area of cornea to be excised will inevitably be followed by the escape of the vitreous through the central corneal wound. This loss of vitreous may be disastrous and be followed by complete collapse of the eye, especially if the vitreous is fluid.

Corneal transplantation in the aphakic eye can be performed successfully, but the operation presents special problems in regard both to the technic employed and to surgical judgment in selecting cases for operation. Many of these cases of opaque cornea in an aphakic eye present the end results of severe complications of cataract surgery, and the decision whether or not the eye should be subjected to further operation must be carefully weighed by the surgeon.

*Types of Opaque Cornea in Aphakia.*—The types of cases which can be considered in this category are: (1) cases of clear cornea that becomes opaque some time after the cataract operation has been done; (2) cases of corneal scarring due to keratitis following post-operative uveitis; (3) cases presenting both interstitial keratitis and mature cataract in which the cataract operation was done first and the resulting vision was not as good as had been anticipated.

1. In cases of the first type are both the corneal opacities that develop in aphakic eyes entirely independent of the condition of aphakia and the opacities that develop in transplantation, which are again unrelated to aphakia.

The many causes of corneal leukoma may occur in the aphakic eye, as well as in the nonaphakic eye, and the resulting impairment in vision must be remedied if at all possible; the same standards for choice of cases for corneal transplantation must be followed for both types of eyes.

Corneal transplants that remain clear for several months are reasonably certain to continue to be transparent; however, clear grafts have been seen to become opaque after a cataract operation has been done. It is known that, owing to systemic disease, trauma, infection or the onset of corneal dystrophy, clear grafts may become opaque at any time and that the opacification be unrelated to the previous operation. An example of this is a case of Groenouw's corneal dystrophy that progressed a number of years after an operation for congenital cataract (fig. 2 *A*). From its onset this condition had progressed, with the typical hyalin-like deposits in the superficial layers of the substantia propria. No vascularization took place, merely a gradually increasing haziness of the cornea developed. This condition indicated the removal

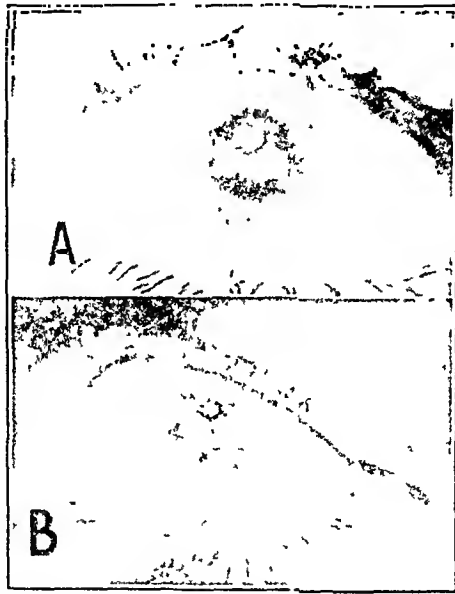


Fig. 2.—*A*, Groenouw's corneal dystrophy in an aphakic eye; *B*, Groenouw's dystrophy following corneal transplantation.

of the opaque cornea in the pupillary region and its substitution by a piece of clear cornea. However, since an intracapsular extraction had been done and examination with the slit lamp revealed the presence of vitreous in the anterior chamber, necessary steps had to be taken to prevent excessive loss of vitreous when the chamber was opened in performing the transplantation. Figure 2 *B* shows the postoperative appearance of this cornea.

I have had several cases of interstitial keratitis in which both corneal transplantation and removal of cataract were successfully performed, but in which at a later date there was reactivation of the interstitial keratitis with infiltration of blood vessels and opacification of the graft. This pathologic change is similar to that shown in figure 1. These

changes necessitate a second corneal transplantation. The choice of cases for the repeat operation requires special attention. One speaks of reoperating for corneal graft, but let it be remembered that the chance of success after corneal transplantation decreases in direct proportion to the number of times the operation is performed.

2. Various degrees of keratitis may follow postoperative uveitis. In most of my cases the condition followed extracapsular operations and the degree of uveitis varied a great deal. The cases in which the uveitis was severe and was associated with extensive vascular infiltration of the cornea fell into the unfavorable group for corneal trans-



Fig. 3.—*A*, dense vascularized scar following deep keratitis; *B*, deep keratitis with infiltration of large vessels.

plantation because of the nature of the infiltrate, and not because the eye was aphakic. In deciding in which of these cases the response to surgery will be good, the general indications and contraindications for corneal transplantation must be kept in mind and the criteria adhered to rigidly. It must be remembered that such cases represent at best the poorest operative risks; consequently, the greatest caution and care must be taken in selecting and preparing the patient when it is felt that benefit may be obtained by operation. Eyes with dense, vascularized scars without an area of fairly clear cornea that can approximate the graft are not suitable for transplantation. Figure 3 *A* illustrates such a case. However, it should be kept in mind that the blood vessels



can be dealt with and obliterated, by means of peritomy, cauterization or beta irradiation. Sometimes all these methods fail to obliterate the blood vessels. Surgeons who have been faced with this complication are well aware of the stubbornness with which the blood vessels resist obliteration. In cases of large, deep, isolated vascular trunks (fig. 3 *B*), I have found it helpful to cut down on these vessels and, with high magnification and the use of two electrodes, positive and negative, to cauterize the vessel directly. Patience and persistence are necessary.

In the cases of less severe uveitis it is often found that the infiltration has progressed somewhat farther toward the center of the cornea than has the vascular infiltration, or relatively clear areas of cornea may remain. In these cases the corneal transplantation can be carried

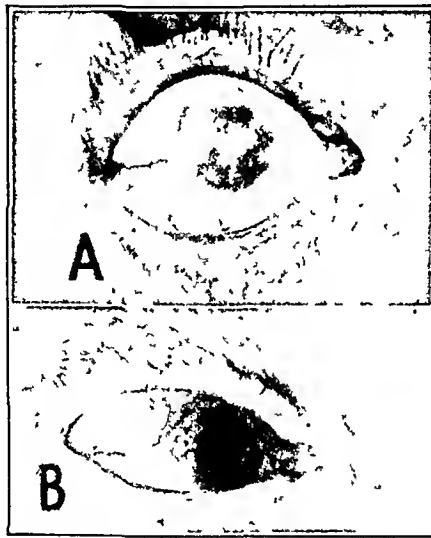


Fig. 4.—*A*, dense avascular corneal scarring following postoperative (cataract) iritis; *B*, eye shown in *A* after corneal transplantation, showing clear central corneal graft.

out after the necessary devascularization has been done. It is also important in these cases to allow a considerable period to elapse after the subsidence of the iritis before attempting the transplantation. Figure 4 *A* illustrates such a case, in which there was diffuse infiltration of the cornea with a relatively clear area in the upper half of the cornea near the limbus. Vascular infiltration of this cornea had not progressed more than 1 mm. beyond the limbus, and this only in scattered areas. Directly below the portion of cornea that is relatively clear was a hole in the posterior capsular membrane.

Corneal transplantation was done on this case, using the technic to be described. No vitreous was lost at the time of operation, and recovery was uneventful. Figure 4 *B* shows the postoperative clear central corneal graft.

In the foregoing types of cases it must be kept in mind that the existing pathologic condition predisposes to the occurrence of glaucoma and that even though this condition does not exist the so-called threshold, or margin of safety, may be narrow and further operative procedure may be enough to induce a condition of increased intraocular tension.

3. There is also the case that presents both a hazy cornea and mature cataract, and the surgeon has to decide whether or not the simpler operation of cataract extraction will be sufficient to restore the patient's

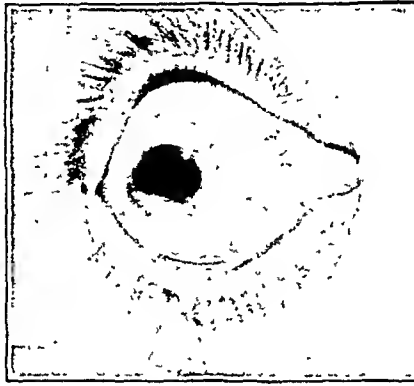


Fig. 5.—Clear corneal graft following transplantation in an aphakic eye.

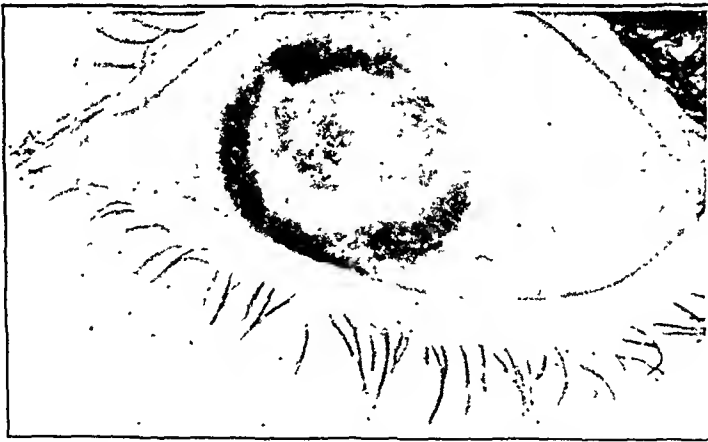


Fig. 6.—Postoperative opaque graft following transplantation in an eye with subluxation of the lens.

vision to a useful level. However, if the patient is not satisfied with the improvement after cataract operation, corneal transplantation must be considered. Such a case is illustrated in figure 5. In this case of trachoma of long standing the interstitial keratitis was not very dense, but vision was improved only to 20/100 after cataract operation. After corneal transplantation vision improved to 20/40, with correction. Figure 5 shows the eye after corneal transplantation.

## DISPLACEMENT OF THE LENS

Surgeons readily know the likelihood of loss of vitreous in removing a subluxated or tremulous lens. The same problem is encountered in performing a corneal transplantation on an eye in which a subluxated lens exists, but the danger of loss of vitreous in these cases is enhanced by the extent of exposure of the anterior chamber and the length of time it remains open in cutting the graft. In most of these cases the diagnosis can be made before a corneal transplantation is done, but occasionally the corneal scarring is dense enough to obliterate the sig-

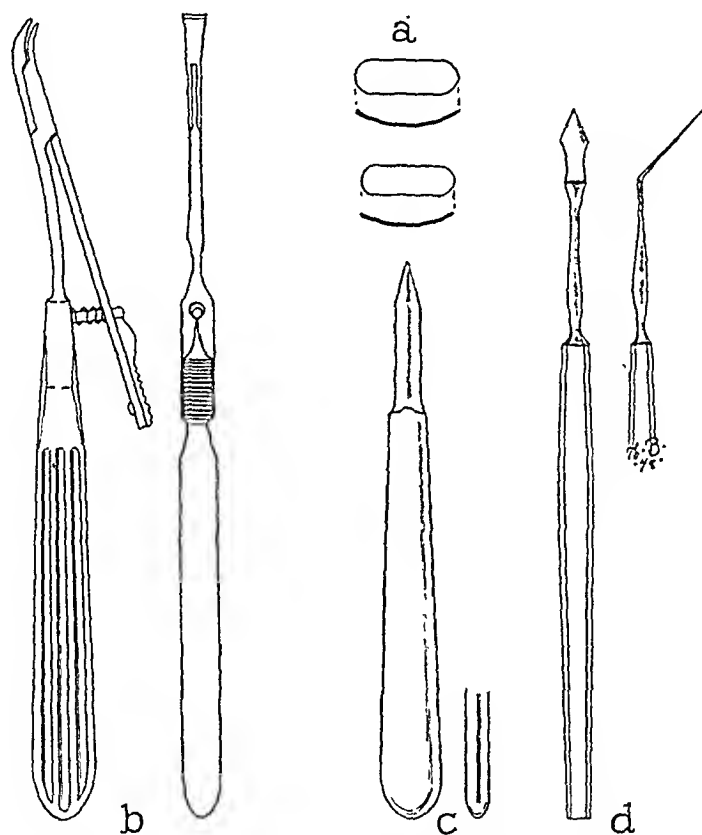


Fig. 7.—Special instruments for corneal transplantation in eyes with aphakia or ectopia of the lens: (a) curved corneal spatulas, (b) holder for spatulas, (c) magnet for stabilization and (d) special keratomes.

nificant clinical signs. When this occurs, the surgeon may not be aware that a dislocated lens exists until the anterior chamber is opened and vitreous presents in the wound. A hurried procedure to lessen the severity of this complication cannot then be carried out. The operation must proceed in the usual manner, but it can be made easier, and the possibilities of success are better, if this complication is prevented. Figure 6 shows a postoperative opaque graft in a case of subluxated lens. This condition was not known to exist until the anterior chamber was opened and the opaque portion to be replaced by graft was in the

process of being removed. Considerable vitreous was lost before the donor cornea was inserted. Of course, the cause of this opacity is open to speculation, and the failure of the graft to remain transparent may have been due to an inherent, incompatible tissue reaction; but in carrying out the precise surgical technic necessary in the corneal transplantation an attempt must be made to minimize every complication. The presence of unexplained opacity in corneal grafts is common enough without any unnecessary complication being added to the surgical procedure.

#### INSTRUMENTS

In order to improve the efficiency of the corneal transplantation operation on the eye in which either aphakia or dislocated lens exists, I devised the instrument presented here. Filatov described a spatula for use in this operation. However, his spatula requires a counter-puncture in the cornea, which is not desirable, and it does not possess a curve which approximates that of the cornea, a feature which insures more secure sealing off of the opening during the grafting.

Figure 7 illustrates the following instruments: (a) two spatulas or blades having an average corneal curve with rounded ends and measuring 6 and 7 mm., respectively, in diameter and 12 mm. in length; (b) a holder for the spatula, having a flat, grasping surface and an easy release mechanism; (c) a magnet for stabilization of blades, and (d) special and 7 mm. keratomes.

The other instruments necessary are the usual instruments for corneal transplantation, which include either the corneal trephine and curved scissors or the double-bladed knife and straight corneal scissors.

#### TECHNIC OF THE OPERATION

Anesthesia is obtained by an injection into the orbicularis muscle and a retrobulbar injection each of 2 cc. of 1 per cent procaine hydrochloride. Tetracaine and cocaine are instilled into the conjunctival sac at two minute intervals for ten doses of each drug. To insure complete dilation of the pupil and to reenforce the preoperative administered atropine, a subconjunctival injection of a preparation containing cocaine hydrochloride (4 minims [0.25 cc.]), 2 per cent homatropine hydrobromide (4 minims) and a 1:1,000 solution of epinephrine hydrochloride (12 minims [0.75 cc.]) is carried out in the perilimbal region of the four quadrants.

The area to receive the transplant is then marked with either the corneal trephine or the double-bladed knife, depending on whether a round or a square graft is to be inserted. This area is then stained with fluorescein sodium. The corneal sutures are inserted in the desired pattern and then drawn back away from the marked edge of the area to be removed. A central suture is inserted into the outlined area, making certain that this suture is deeply and well placed, as traction is necessary to remove the area satisfactorily. It is easier to cut the area out of its bed if the initial corneal markings have been carried rather deep into the cornea.

A small conjunctival flap is dissected free at the limbus on a line with the central area to be removed, and a corneoscleral suture is inserted at this limbal region. Either the 6 or the 7 mm. special keratome is then introduced and an incision the width of the keratome is made. On withdrawal of the keratome, the anterior

chamber is usually lost with the overflow of aqueous. The desired spatula or blade, corresponding in width to the keratome used, is then inserted into the special holder and this put through the limbal incision to the opposite side of the anterior chamber and placed firmly against this angle. The handle then releases the blade, and its free end can be steadied, if necessary, by the use of the handle magnet placed over the limbus. This may or may not be necessary, depending on the apparent stability of this spatula. Care must be exerted to keep close to the posterior surface of the cornea in inserting this blade so as to prevent

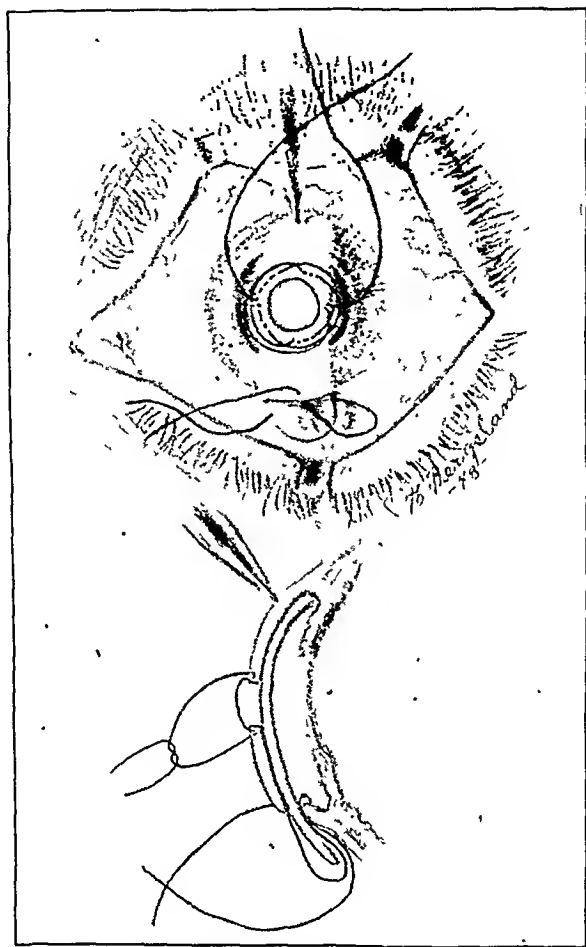


Fig. 8.—Drawing with spatula in the anterior chamber and the central area of cornea removed, ready to receive the graft. The cross section shows how securely the opening is blocked.

damage to whatever structures lie beneath. Its location must also be directly underneath the area of cornea to be removed.

The area of cornea to be removed is excised by first introducing a small cataract or discission knife along the marked border. After the incision is begun it is completed by the use of the special corneal scissors. When this central area is removed, it will be noted that the spatula is immediately underneath and blocking this opening, thereby preventing the overflow of vitreous, which otherwise would escape freely (fig. 8). The magnet applied to the limbus over the free end of the spatula holds this upward and firmly blocks the opening in the cornea

The donor cornea is cut in the usual way and replaces the area removed from the recipient cornea. The corneal sutures are then drawn over the graft, and the blade or spatula is withdrawn, using the special holder (fig. 9). The corneo-scleral suture at the limbus is then drawn tight and the wound is closed. Atropine and an antiseptic ointment are instilled into the eye, and a dressing is applied. It is advisable to cover both eyes after this operation.

In some cases of aphakia and leukoma, the iris is often immobile and cannot be dilated very well. This condition was found to be present in the case illustrated in figure 3*B*. Consequently, in order to help reform the anterior chamber and

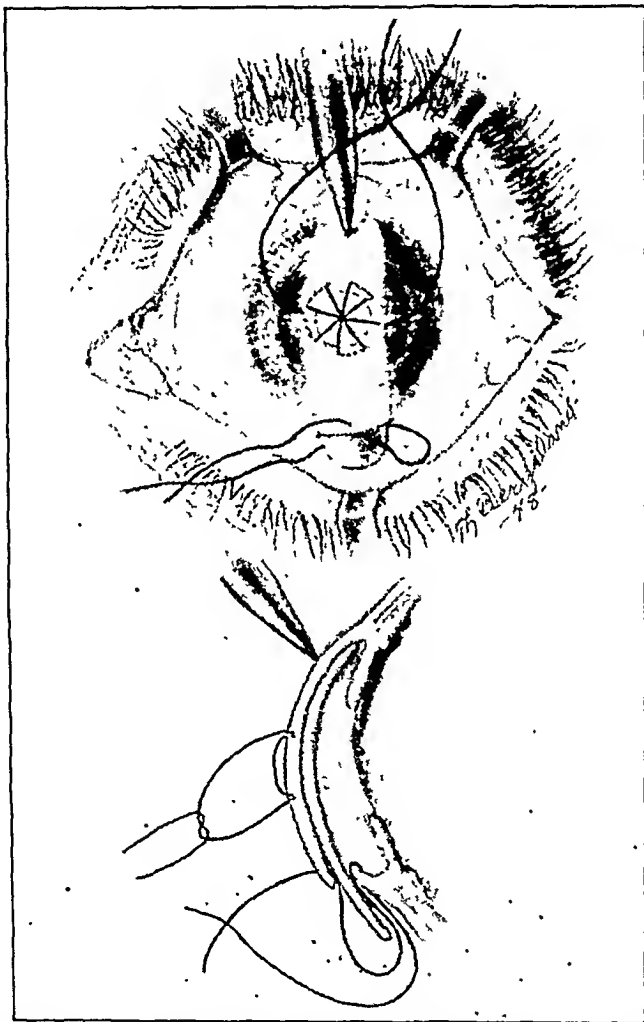


Fig. 9.—Drawing after graft has been inserted and the sutures have been tied. The spatula is now ready to be withdrawn.

prevent any anterior synechia, as the iris usually lies directly beneath the corneal wound, one may inject a small amount of isotonic solution of sodium chloride into the anterior chamber through the corneoscleral wound, previously closed.

The advantages of this instrument (spatula) are as follows:

1. The spatula is easy to manage. By means of the special holder, it can be introduced into the anterior chamber very much as one would insert a keratome. It can be kept in complete control until it has

reached the opposite angle of the chamber and is then easily released. Its stability and efficiency are enhanced by the magnet, which holds the free end upward against the cornea.

2. No counterpuncture is necessary for fixation. This necessitates a smaller corneal incision and lessens interference in metabolism and nutrition of the corneal graft.

3. The curve of the spatula more or less simulates that of the cornea, so that the spatula lies in close proximity to the inner surface of that structure. This, of course, tends to block any exit of intraocular fluid, which is the sole purpose of the feature.

4. The blades or spatulas that are introduced into the anterior chamber are of the exact same size as the keratomes used in making the incision. This provides for a tight fit around the end of the spatula and prevents unnecessary leakage of vitreous or of fluid from the anterior chamber.

Pitfalls of the operation are two:

1. Difficulty in cutting the recipient cornea. In removal of the area to be replaced by the graft, the initial puncture into the anterior chamber presents some difficulty, as the puncture must be made on a soft eye and, consequently, resistance is offered only by the traction upward by means of the central corneal suture and the very slight cutting resistance of the spatula in the anterior chamber. When the scissors can be introduced, the remainder of the cutting is relatively simple.

2. Prolapse of the iris. It is imperative to secure maximum dilation of the pupil before operation, for after the spatula is inserted the iris cannot be seen until after the operation is completed and the spatula is withdrawn. If the iris becomes incarcerated, its repair must wait until another time, when it can be freed by the method described by Castroviejo.<sup>6</sup> It apparently may be free immediately after operation but become incarcerated when the first dressing is done, forty-eight hours later. It is forcefully recommended, therefore, that the operation be preceded by instillation of sufficient atropine and a subconjunctival injection of a mydriatic at the time of operation.

#### COMMENT

The choice of cases of aphakia which are favorable for operation requires good judgment and a great deal of experience on the part of the surgeon. The case with a subluxated lens does not present this special problem.

The ideally favorable type of aphakia for operation is the interstitial keratitis of systemic origin that may become active after the cataract operation has been performed, but in which vascularization recedes

rapidly and completely, or the corneal leukoma of external origin that may follow ulceration or trauma.

The aphakic eye with little vascular infiltration may present no special problem or preoperative preparation. It is the aphakic eye with vascular infiltration and deep scarring that may require special attention and preoperative preparation. These eyes are often borderline candidates for glaucoma, a fact which should constantly be kept in mind. Then, again, further operative procedures may reactivate the underlying keratitis and the transplantation would probably be followed by failure, due to opacity of the graft.

Corneal grafts become opaque at times for inexplicable reasons, and it is necessary for the best results that the surgeon exercise all the means at his disposal to prevent this result through proper choice of cases and the minimizing of mechanical difficulties.

#### SUMMARY

Experience with corneal transplantation in cases of aphakia or displaced lens is summarized as follows:

(a) In cases of combined corneal leukoma and cataract the corneal transplantation should be done before the cataract is removed.

(b) Corneal transplantation can be performed on aphakic eyes that are properly selected and prepared, and when proper instrumentation is used for the operation.

(c) Ectopia of the lens also presents the problem of loss of vitreous, which must be prevented for the best results.

2. Instruments are shown and the technic is outlined for corneal transplantation in either the aphakic eye or the eye with ectopia of the lens.

3. The advantages of the instruments are outlined and the pitfalls of the operation stated.

Mr. Karl Kapp gave help in making these special instruments.

The instruments described are available through V. Mueller & Co., Chicago.  
10515 Carnegie Avenue.



# RELATION OF COLOR SENSITIVITY IN THE VISUAL FIELD TO THE LAMINAR PATTERN IN THE LATERAL GENICULATE BODY

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A DETAILED study of the laminar organization in the lateral geniculate body of primates has been presented in an earlier paper.<sup>1</sup> In the present paper an attempt will be made to relate the distribution of color sensitivity in the visual field to the laminar pattern in the human geniculate nucleus.

The distribution of the transneuronal degeneration in the lateral geniculate body after localized retinal lesions, affecting portions of all three cell laminae related to each eye, has led to the inference<sup>2</sup> that the conducting unit in the optic nerve and tract from the retina is a three fiber unit. It has also been suggested<sup>3</sup> that the three fiber unit and the trilinear pattern in the geniculate body may have a relation to the three fundamental colors of the Young-Helmholtz color theory. Some of the indirect evidence in favor of this thesis has been presented elsewhere.<sup>4</sup> It is of considerable interest at this point to utilize the recently obtained data on the human geniculate body in an attempt to correlate the regional variation in the laminar pattern with the distribution of color sensitivity in the visual field.

A close scrutiny of the distribution of the foci of secondary degeneration as depicted in the illustrations of Clark and Penman<sup>2</sup> reveals that a lesion in the peripheral retina was always followed by degeneration in one of the two sets of two cell laminae which constitute the projection zone of peripheral vision in the geniculate body. It may be argued, therefore, that if the conducting unit from the central area of the retina is a three fiber unit, that from the peripheral retina is a two fiber unit. If the postulation of a relation between a three fiber unit and trichromatic vision is permissible, it seems permissible also to consider a relation between a two fiber unit from the peripheral retina and dichromatic

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vision. These suggestions, which have grown out of the experimental work on monkeys, appear equally applicable when one is considering the human lateral geniculate body, since the projection areas for peripheral vision in man are also composed of two sets of two cell laminae (each set being related to one eye). Other relevant anatomic observations on the retinal projection areas in the human geniculate body which now seem well established may be summarized as follows:

1. In the projection area for central vision of the human lateral geniculate body there are, in general, two sets of three laminae, each set belonging to one eye and consisting of one large cell layer and two small cell layers. The conducting unit, originating in the area for central vision of the retina of one eye and terminating in one geniculate nucleus, is a three fiber unit.
2. In a certain region of the area for central vision in monkeys, an extradifferentiation (splitting) of the fourth and fifth layers may be observed. An extradifferentiation is also seen in man, although it may assume a different pattern. These observations suggest, therefore, a tendency to evolve even a four fiber unit.
3. At the foveal center, the large cell elements being few or absent altogether, there are two sets of only two laminae, each set belonging to one eye and consisting of two small cell layers. The conducting unit in this case is a two fiber unit.
4. In the area for peripheral vision there are two sets of two laminae, each set belonging to one eye and consisting of one large cell layer and one small cell layer. The latter represents a composite layer formed by the fusion of the two small cell layers of the area for central vision. The conducting unit from each eye is, therefore, a two fiber unit, although of a type different from that in the center for foveal vision.
5. In the area for monocular vision the laminae and cells lose their distinctive features to a certain extent. This area may be considered the least differentiated part of the geniculate nucleus. The laminae are related only to the opposite eye, the uncrossed laminae being excluded from this region. The conducting unit originating in one eye is a two fiber unit.
6. The conducting fibers originating in the central portion of the retina and terminating in the large cell laminae appear to be relatively few, while those from the peripheral retina are predominant.
7. From an analysis of the experiments of Clark and Penman<sup>2</sup> it may be inferred that the smallest localized lesion in the retina results in transneuronal degeneration, the area of which is limited to a wedge-shaped region extending through the whole dorsoventral thickness of the lateral geniculate body. The number of laminae in the area thus affected depends on the position of the lesion in the retina. This means

that each locus on the retina is projected not on a point on the geniculate body, as the term "point to point" projection implies, but on a pyramidal slice of the nucleus. In the area of central vision in the nucleus, the apex of the pyramid is ventrally placed and directed toward the hilus, the large cell laminae being placed at this end of the pyramid. Layer 6 is located at the dorsally situated base of the pyramid. Such a portion of the geniculate body may be arbitrarily referred to as a "unit." Each such "unit" is then related to two corresponding points on the retinas of the two eyes. It always contains two sets of laminae, a "crossed" set, related to the point in the contralateral eye, and an "uncrossed" set, related to the point in the ipsilateral eye. The two sets contain the same number of laminae.

8. A characteristic mode of distribution of cells in the nucleus becomes manifest when the size of the cells in the various laminae is determined. Such a study<sup>5</sup> has revealed a regular cell size gradient in the laminae of the various projection areas of the geniculate body. For instance, the larger the size of the cells, the more numerous they are in the more ventrally placed laminae. The larger cells steadily decrease in number in the more dorsally placed laminae. The reverse is the case with the relatively smaller size cells in their distribution in the various layers. It follows from these data on the cell size gradient that the two sets of laminae (the "crossed" and the "uncrossed") comprising a single "unit" are not exact replicas of each other. The laminae of the two sets are so fitted together that they present the picture of a composite whole in each "unit," with transitions and continuous gradations. This means, for instance, that the size characteristics in one of the two sets of the three laminae related to one eye in the area for central vision are such that the complete picture of the continuous and finer gradient in the "unit" appears only if the gaps are filled in through the second set of laminae, related to the corresponding half of the other eye. Since the total number of laminae in any one "unit" in the various projection areas of the geniculate body represents the full quota of the constituent parts of the "unit" if the latter is to function with full efficiency in binocular vision, it is advisable to speak of an eight or a six fiber unit in the area for central vision, a possible four fiber unit in the foveal center, a four fiber unit of a different type in the area for peripheral vision and a two fiber unit in the area for monocular vision.

Turning from the anatomic data to a consideration of the regional variations in color sensitivity in the normal retina, I shall make special mention of some of the pertinent data available in the literature. Most observers obtaining data on the color sensitivity of the human retina have found that green and red are perceived only for a relatively

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5. Chacko, L. W.: *J. Anat.*, to be published.

short distance beyond the fovea and that the fields for blue and yellow extend farther out into the periphery. Ferree and Rand,<sup>6</sup> who used monochromatic lights of equal energy contents, concluded, however, that the visual fields for red, blue and yellow occupy the same area and that this area is less restricted than the field for green. Abney,<sup>7</sup> who also used spectral colors, found, under conditions of low or moderate illumination, that the fields for color vision increased in size in the following order: green, red, yellow and blue. A red-green mixture which matched yellow in hue and luminosity was found to have a considerably smaller field than pure yellow itself. Baird<sup>8</sup> tested the color sensitivity of the peripheral retina by recording the changes in color perception from the periphery of the retina toward the center. Red appeared yellow at the periphery and, passing through yellow-orange, was finally seen as red at the center. Green appeared yellowish at the periphery and gradually passed through greenish yellow to green. Yellow appeared as yellow throughout the transition but increased in saturation toward the center. A similar result was obtained with blue. Although it is not easy to equate the results of different observers, the consensus seems to be that, in contrast to the trichromasy of the central area of the retina, the periphery (at least under moderate degrees of illumination) shows dichromasy for blue and yellow. One may also mention the low sensitivity to blue at the center of the fovea, observed by Willmer<sup>9</sup> and others. Willmer assumed that the center is actually blue blind, owing to the absence of blue receptors. Thomson and Wright,<sup>10</sup> in their color-matching experiments, found an increase of sensitivity to blue light when the matching field was moved from the center toward the edges of the central fovea. Charpentier<sup>11</sup> published curves showing the sensitivity to colors in different parts of the field of vision. His curve for blue takes a sudden dip as it approaches the fixation point, indicating a lower degree of blue sensitivity in that region.

The question now arises: Has the regional variation in color sensitivity any relation to the structural characteristics of the geniculate body? Are there certain features of the laminar organization or of the cellular or synaptic morphology which contribute to a structural foundation for color perception? On the basis of the principle of a "point to point" projection an analysis of the relevant functional and anatomic data sug-

6. Ferree, C. E., and Rand G.: *Am. J. Ophth.* **3**:772, 1920.

7. Abney, W. de W.: *Colour Vision*, London, 1895, Longmans, Green and Co.

8. Baird, J. W.: *The Color Sensitivity of the Peripheral Retina*, Washington. D. C., Carnegie Institution, 1905.

9. Willmer, E. N.: *Retinal Structure and Colour Vision*, London, Cambridge University Press, 1946.

10. Thomson, L. C., and Wright, W. D.: *J. Physiol.* **105**:310, 1947.

11. Charpentier, A.: *La lumière et couleurs au point de vue physiologique*, *Compt. rend. Soc. de biol* **8**:308, 1888.

gests the following correlations: The less distinct lamination of the narrow strip of the area for monocular vision is related to achromatic vision or to light sensations manifesting themselves as gray devoid of other specific chromatic attributes; the area for peripheral vision of the geniculate body, with its two sets of two laminae, is related to the color sensitivity of the peripheral retina, which confines itself chiefly to the blue and yellow regions of the spectrum; the area for central vision, with its greater differentiation into from six to eight laminae, is related to perception of colors comprising a larger range of the spectrum and a greater ability to recognize and discriminate various hues. The fact that at the foveal center the large cell layers of the geniculate body appear to contribute only a very small portion of the area for central vision, and, indeed, may be completely absent, lends itself to the interpretation that the large cell layers are related to blue perception. This interpretation seems to gain further support from clinical cases of toxic amblyopia reported by Rönne.<sup>12</sup> In these cases the degeneration of the papillomacular bundle, resulting in a central scotoma, was associated with a localized area of transneuronal degeneration in the lateral geniculate body. Particularly apposite are Rönne's cases of diabetic amblyopia, in which the color defects were perimetrically charted. It is generally known that in the milder forms of toxic amblyopia the sensitivity to green and red diminishes and disappears first whereas the sensitivity to yellow and blue remains undisturbed; with severe forms, perception of yellow and blue also becomes affected (Samelsohn, Rönne, Abney, Traquair, Duke-Elder). Thus, in Rönne's first case of diabetes there was complete loss of green perception for the total field, in addition to a central scotoma for red. In the second, severe case, perception for both green and red was lost, while the field for blue was intact except for a very small central scotoma for white. In the geniculate bodies in these cases, the small cell layers of the area for central vision had undergone profound degeneration, whereas the large cell layers were intact throughout their extent. The coincidence of the sparing of blue perception and the maintenance of the integrity of large cell elements is striking.

As regards the relation of the neural elements of the retina and the laminar pattern of the geniculate body to color vision, little has as yet been definitely established. Polyak<sup>13</sup> drew attention to the varieties of bipolar cells found in the retina and argued that, since maximum brightness of scotopic vision, as well as the maximum absorption and bleaching of visual purple of the rods, is concerned with the short wave portion of the spectrum, it is legitimate at least to hypothesize that the bipolar varieties related to the rods mediate impulses elicited by light

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12. Rönne, H.: *Arch. f. Ophth.* **77**:1, 1910; *ibid.* **85**:489, 1913.

13. Polyak, S. L.: *The Retina*, Chicago, University of Chicago Press, 1948.

of shorter wavelengths, e. g., mop bipolar cells, and that the bipolar forms related to the cones transmit impulses preponderantly initiated by light of long and medium wavelengths. According to Polyak, the brush and flat bipolar cells, related to varying proportions of rods and cones, may be concerned with impulses elicited by the portion of the spectrum between green and violet. He emphasized the relation of the brush and flat bipolar cells to green and of mop bipolar cells to blue and violet. Similarly, he stated the belief that the midget bipolar cells presumably mediate impulses elicited by the long wave portion of the spectrum, approximately from red to green, with a probable emphasis on red. In connection with these suggestions, it is to be noted that the mop variety of bipolar cells is absent from the foveal center and that the midget bipolar cells are cruder and fewer in the extra-areal periphery of the retina.

With regard to the third neuron of the retina, the ganglion cells, one may summarize Polyak's histologic observations by saying that the larger these cells are, the thicker are their dendrites, the broader their dendritic expansions and the greater their number toward the periphery of the retina. Despite the complexity of the synapses in the retina, the neurons of a rod-dominated path form convergent pathways in a central direction and are of relatively larger size; it appears legitimate therefore to assume that the large ganglion cells, on account of their location in the course of a rod-dominated path, mediate impulses elicited by light chiefly of shorter wavelengths. On the other hand, the midget ganglion cells, establishing monosynaptic connections with midget bipolar cells, and through the latter with cones, may be concerned mainly with light of longer wavelengths. Polyak also stated that the thickness of the axons of the ganglion cells is commensurate with the size of the cell body, the larger ganglion cells having thicker axons. The large cells of laminae 1 and 2 of the lateral geniculate body are also found to have thicker axons and dendrites. Such facts and considerations seem to support a correlation between the large ganglion cells of the retina and the large size cells of laminae 1 and 2 of the lateral geniculate body. This tentative correlation is supported by the histologic details of Rönne's<sup>12</sup> cases of amblyopia, for he noted a selective degeneration of small (midget) ganglion cells in the fovea, whereas the large ganglion cells (which are also present in the fovea, but in the minority) were intact. As already noted, in these cases the degeneration in the geniculate body was confined to the small cell layers, the large cell layers being left unaffected. The importance of this observation of Rönne cannot be too strongly emphasized, in view of the fact that it is not practicable to bring about such selective atrophy by experimental methods in order to determine the specific connections between the third and the fourth neuron of the visual path. Thus, it

seems possible that the large ganglion cells in the retina are linked with the large cells in laminae 1 and 2 of the lateral geniculate body and that the latter are situated principally in the rod-dominated pathway of the visual system and therefore possibly mediate impulses elicited by light of shorter wavelengths. If it is assumed that in the projection zone for central vision of the geniculate body the large cell layers related to each eye subserve the blue region of the spectrum, the dorsally situated laminae, in which smaller cells are in the majority, may mediate impulses elicited by the longer wavelengths and the intermediate laminae may mediate impulses from the middle portion of the visible spectrum. The observed fusion of the third layer with the fifth and of the fourth layer with the sixth in the projection zone for peripheral vision might be considered as related to yellow, but not to red and green separately; in other words, it might be assumed that the impulses from the red and green receptors, even if the latter were present in the peripheral zone of the retina, would no longer remain segregated at the geniculate level or beyond it. If the thesis that the laminae of the geniculate body mediate impulses elicited by different portions of the visible spectrum is substantiated, the greater differentiation into extra laminae would imply the development of a mechanism to subserve finer gradations of hue.

Electrophysiologic investigations may throw light on this problem. Of special importance are Granit's<sup>14</sup> extensive studies on the spectral sensitivity of the retina. In a large series of experiments, he recorded potentials from one or a few fibers of the optic nerve. His results indicate that the receptors and neurons associated with a particular optic nerve fiber, while being sensitive to all parts of the visible spectrum, have a specific maximum sensitivity. Furthermore, it appears probable that further specificities are introduced by virtue of the fact that the optic nerve fibers from the different portions of the retina vary in caliber<sup>15</sup> from 0.7 to 10 microns. The differences in records of potentials as picked up from various optic nerve fibers depend on the wavelength of the stimulating light, on the sensitivity of the particular retinal elements stimulated and on the particular optic nerve fiber contacted for picking up the potentials. Thus, Granit's observations have led to knowledge of the spectral sensitivity of retinal elements connected with different optic nerve fibers. The optic fibers conducting impulses from retinal elements with specific sensitivity are sorted out when approaching the geniculate body and terminate in certain specific fields in it. These fields are the laminae, which, as has previously been indicated, are characterized by certain morphologic characteristics. The sum total

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14. Granit, R.: *Sensory Mechanisms of the Retina*, London, Oxford University Press, 1947.

15. Chacko, L. W.: *Brit. J. Ophth.* **32**:457, 1948.

of activity of a particular lamina, then, will depend not only on its own special characteristics, but also on the number, quality and retinal connections of the optic nerve fibers terminating in it. In the light of these considerations, it appears likely, therefore, that the total activity of a particular lamina is concerned only with such events as are initiated by stimulation with light of a limited spectral range.

Although the observations reported here have been assembled in support of the thesis that the laminar pattern in the lateral geniculate body of the primates has a specific relation to color vision, evidence is only indirect and presumptive. Further evidence must be sought in four directions: (1) a study of localized electrical responses in the geniculate body following stimulation of the retina by light of different wavelengths; (2) a systematic charting of the primate retina utilizing Granit's electrophysiologic technics, as previously employed in the study of other mammalian retinas; (3) further research on the effects of prolonged exposure to monochromatic light leading to selective laminar degeneration, and (4) a detailed analysis of further clinical cases with color scotomas or color blindness.

Prof. W. E. L. Clark, Prof. S. Polyak and Prof. H. Klüver offered a critical discussion of the subject and gave help in the preparation of this paper.

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## RHEUMATOID INVOLVEMENT OF THE EXTRAOCULAR MUSCLES

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THE DIAGNOSIS of rheumatic disease of the eyes was made with great frequency in the past. It has slowly been relegated to obscurity as more specific etiologic factors in disease have been uncovered. At present, it represents a "wastebasket" diagnosis, hard to substantiate and made only infrequently, and the etiology is unknown.

The association of inflammation of the episclera and sclera with diseases of the articular structures of the body was reported by Hutchinson<sup>1</sup> in 1885, by Fuchs<sup>2</sup> in 1895 and by Wangenmann<sup>3</sup> in 1897. Verhoeff and King<sup>4</sup> reported a case of a perforating scleral lesion associated with rheumatoid arthritis; these authors discussed similarly reported cases of a condition designated as scleromalacia perforans. Smoleroff<sup>5</sup> reported 3 cases of advanced rheumatoid arthritis and scleral nodules; the pathologic changes were deep abscesses in the sclera.

Kneis<sup>6</sup> referred to rheumatism as the etiologic factor in iritis, cyclitis, tenonitis, keratitis, optic neuritis and rheumatic paralysis. Fuchs mentioned rheumatism frequently as an etiologic factor in sclerosing keratitis, scleritis posterior, iritis and tenonitis. Of the last condition, he stated: "The causes of tenonitis are still obscure; one makes gout, rheumatism and exposure to cold responsible as etiologic factors." The disease tends to recur and does not leave behind any permanent results.

Babel<sup>7</sup> reported histologic changes in the eye in a man aged 35 who died of rheumatic myositis. There was involvement not only of

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1. Hutchinson, J.: *Tr. Ophth. Soc. United Kingdom* 5:1, 1885.

2. Fuchs, E.: *Diseases of the Eye*, authorized translation by E. V. L. Brown from fifteenth German edition of "*Lehrbuch der Augenheilkunde*," Philadelphia, J. P. Lippincott Company, 1932, p. 197.

3. Wangenmann, A.: *Arch. Ophth.* 43:83, 1897.

4. Verhoeff, F., and King, M. S.: *Scleromalacia Perforans*, *Arch. Ophth.* 20:907 (Dec.) 1938.

5. Smoleroff, J. W.: *Scleral Disease in Rheumatoid Arthritis: Report of Three Cases, in One of Which Both Eyes Were Studied Post Mortem*, *Arch. Ophth.* 29:98-108 (Jan.) 1943.

6. Kneis, M.: *Relations of Diseases of the Eye to General Diseases*, New York, W. Wood & Company, 1895, p. 372.

7. Babel, J.: *Contribution à l'étude histologique du rhumatisme oculaire*, *Ophthalmologica* 104:243-253 (Nov.) 1942.

the sclera, Tenon's capsule and uvea, but also of the external muscles of the eye, which showed a characteristic myositis with nodules. The same changes were noted in the myocardium, endocardium and synovial membranes. In a series of 105 cases of rheumatic fever carefully studied by Rudolph, no ocular abnormalities were found.

The case to be reported is one in which there was intimate association of recurrent ocular inflammation with generalized bouts of a rheumatoid syndrome.

#### REPORT OF A CASE

*First Attack.*—B. B., a white girl, was first observed in November 1940, at the age of 9 years. At that time she complained of severe headaches over the left eye. Diplopia followed two weeks later; the left eye was completely immobile in its excursions and was fixed in the primary position. The eyeball was white, with no apparent inflammatory process of the anterior portion of the sclera or episclera. There was no exophthalmos. Over a period of ten weeks the pain and diplopia disappeared.

*Second Attack* (November 1941).—*Right Eye:* The patient had been free from symptoms for one year, when the right eye became involved. There were some

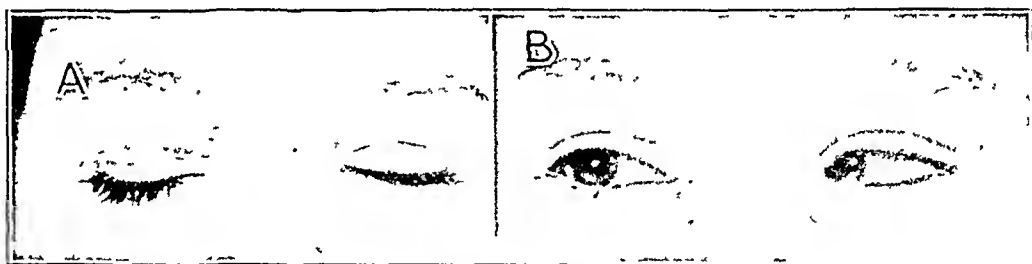


Fig. 1.—(A) Proptosis and edema of the upper lid and (B) poor abduction of the right eye during the second attack.

edema of the upper lid, slight chemosis and proptosis and mild pain (fig. 1 A). Diplopia was present and increased on her looking into the field of the right lateral rectus muscle; the diplopia was not due to refusal to use this muscle because of pain. The ocular excursions were normal except for poor abduction of the right eye (fig. 1 B). On the Hertel exophthalmometer, the right eye measured 18 mm. and the left eye 15 mm. The edema of the lid, as well as the chemosis, pain and exophthalmos, disappeared rapidly. However, the diplopia remained the most prominent feature. As time progressed, the superior oblique, the medial rectus and then the superior rectus muscle became involved in that order, with diplopia increasing in the field of each muscle as it became affected.

The temperature ranged about 100 to 101 F. for four weeks. The sedimentation time was considerably increased, measuring 24 mm. in thirty minutes. Erythema nodosum was present for two weeks, associated with migratory polyarthritis (fig. 2). The electrocardiogram was normal. *Escherichia coli* was cultured from the urine. A patch test gave a negative reaction to tuberculin. Examination of a peripheral blood smear revealed mild leukocytosis, with 15,000 white cells, 74 per cent of which were polymorphonuclear leukocytes and 26 per cent lymphocytes.

The patient made a gradual recovery over a period of eight weeks. She was completely free of diplopia and all other symptoms until July 1942.

*Third Attack* (July 1942).—*Right Eye*: The right eye was then involved, with diplopia the most prominent feature and with some edema and pain. This episode lasted six weeks.

*Fourth Attack* (January 1943).—*Left Eye*: The patient was free from symptoms between attacks. This episode involved the left eye and necessitated hospitalization for four weeks.

*Fifth Attack* (July 1943).—*Left Eye*: After an interim of six months, during which the patient was free of diplopia and all symptoms, the left eye became involved with diplopia and some pain. Massive doses of thiamine hydrochloride were given, without apparent effect

*Sixth Attack* (July 1945).—*Left Eye*: Until this episode, the patient had been free of symptoms for two years. There was mild edema of the upper and lower lids of the left eye, accompanied with severe pain. Visual acuity was 20/20 in



Fig. 2.—Erythema nodosum.

each eye with correction. Marked tenderness was present on palpation over the orbital rim in the region of the trochlea of the superior oblique and over the periosteal attachments of the inferior oblique. Diplopia was present in the fields of action of these two muscles. The fundi were normal. During the first two weeks of this attack, the pain subsided, but the diplopia kept increasing in the fields of the oblique muscles. Fulness appeared in the lower lid, and a mass could be felt in the region of the periosteal attachment of the inferior oblique as the patient looked upward; this was thought to be a swollen inferior oblique muscle. With the Hertel exophthalmometer, the left eye measured 16 mm. and the right eye 14 mm. of exophthalmos. There were no abnormalities of the visual fields. The intraocular pressure was normal. Clinically, the paranasal sinuses were free of any pathologic condition. Roentgenographic examination of the skull and sinuses failed to reveal any abnormalities. The optic foramina were within normal limits of size and form. General physical examination revealed nothing abnormal. Cutaneous tests showed that the patient was allergic to chestnuts, walnuts, apricots,

pumpkin and hog's hair. The temperature ranged around 98 F., and there was no elevation of the pulse rate. Examination of the blood revealed 4,200,000 red cells, with 13.3 Gm. of hemoglobin per hundred cubic centimeters and 7,000 white cells, 52 per cent of which were polymorphonuclear leukocytes, 44 per cent lymphocytes and 4 per cent monocytes. The basal metabolic rate was -14 per cent. Intramuscular administration of large doses of penicillin was apparently without response. The diplopia slowly decreased over a period of eight weeks.

*Seventh Attack* (Oct. 1, 1945).—Right Eye: The patient was free from symptoms and without diplopia for four weeks, when the right eye became affected. There was mild edema of the upper lid (fig. 3). During this episode the superior oblique and then the superior rectus muscles were involved, with pain on looking into the field of each muscle and tenderness to palpation of the globe over the affected muscle. As involvement of these two muscles subsided, the medial rectus muscle became affected.

Two weeks after the onset of this episode, one could palpate several tender subcutaneous nodules in the scalp in the occipital region. It was found that the muscles of the back of the neck were tender. A transitory period of migratory polyarthritis involved the right ankle, both wrists and the metacarpophalangeal



Fig. 3.—Edema of the upper lid of the right eye and paresis of the internal rectus muscle during the seventh attack.

joints of the right hand. These joints were red, hot, swollen and painful to movement and palpation. Erythema nodosum was present for four days. The temperature ranged from 98 to 101 F. The peripheral blood smear was normal, with no eosinophilia. Biopsy of an excised subcutaneous nodule from the scalp revealed nonspecific fibrosis.

*Subsequent Course.*—During 1946 there were occasional transitory episodes of diplopia associated with migratory polyarthritis. On Feb. 2, 1946, paresis of the left superior rectus muscle was noted. This subsided rapidly, and on Feb. 13, 1946 the left inferior rectus muscle was found to be paretic. No sooner had the diplopia been overcome than the left inferior oblique was found to have been affected (fig. 4). In July 1946 there was spontaneous diplopia in the position of eyes left beyond the midline and in the lower fields below 30 degrees. Paresis of the right superior oblique could be mapped out with the cover test (fig. 5A). Diplopia disappeared gradually over a period of four weeks. At the last examination, on Jan. 3, 1947, no diplopia could be elicited with the red glass test; only traces of hyperphoria were present (fig. 5B). Except for pronounced fatigue, the patient was free of complaint. During 1947 and 1948, the patient resided in Southern California and had no attacks.

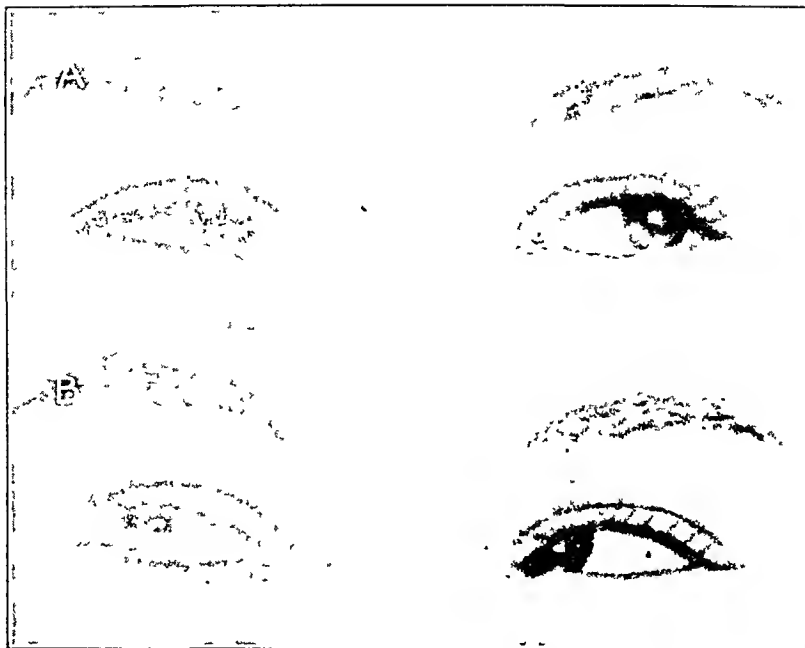


Fig. 4.—*A*, paresis of the left superior rectus; *B*, paresis of the left inferior oblique

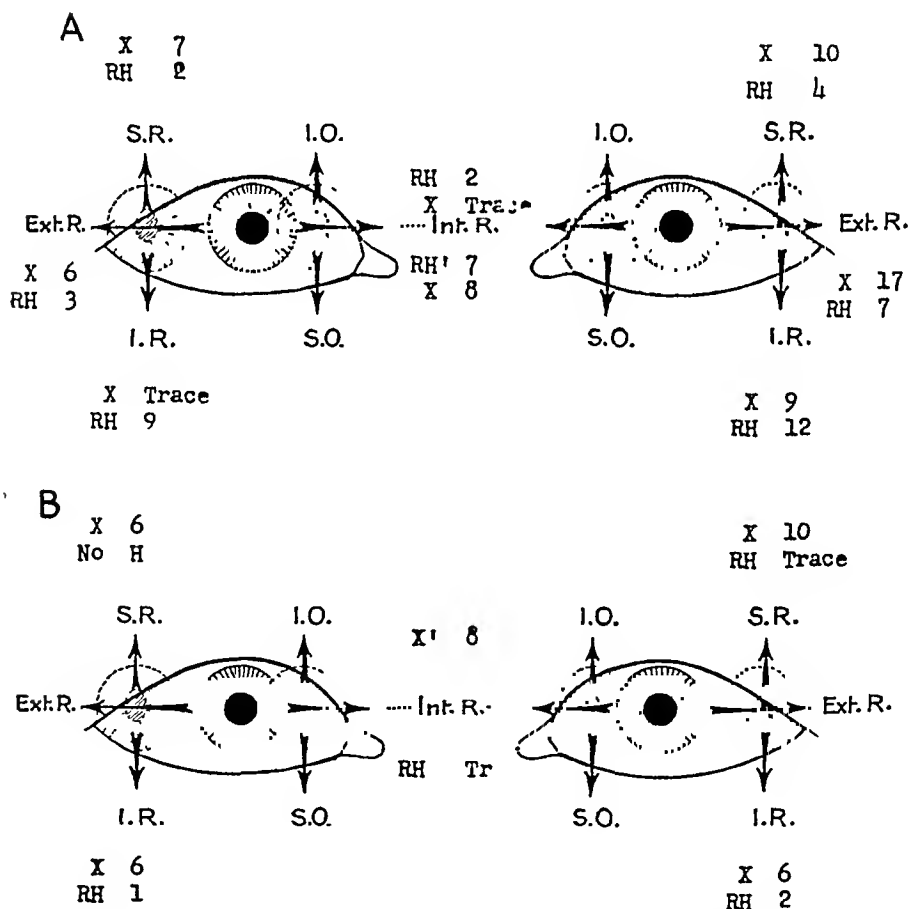


Fig. 5.—*A* (July 26, 1946), spontaneous diplopia to the left and beyond the midline in the lower fields; paresis of the right superior oblique muscle. *B* (Jan. 3, 1947), no diplopia as tested with the red glass. Paresis of the right superior oblique muscle has subsided. Charting was done on the diagnostic card designed by Dr. J. W. White, New York.

## COMMENT

The most prominent feature in this case was diplopia. During an acute attack double vision could be mapped out, the diplopia being due to paresis of individual muscles and increasing in the field of action of the particular muscle. There was pain on looking into the field of the paretic muscle, with tenderness to palpation over it. Without question, Tenon's capsule was involved in several episodes, as manifested by the exophthalmos, edema of the lids, chemosis and pain. However, the involvement of the external ocular muscles appears to have been the most prominent feature and is of interest from the point of view of complete remissions and the ability to overcome the diplopia by fusion. There was repeated association of ocular involvement with migratory polyarthritis, erythema nodosum, fever, rapid sedimentation time and subcutaneous nodules. It appears that the extraocular muscles were affected by a transitory inflammatory process, the cause of which was the same as that producing the generalized rheumatoid syndrome.

## SUMMARY

A case is reported of repeated episodes of diplopia with remissions in which the diplopia was overcome by fusion.

These episodes were associated with a generalized rheumatoid picture.

The ocular involvement was probably on a rheumatoid basis.

The repeated inflammatory process of the extraocular muscles was the most prominent feature of the ocular picture.

# INFLUENCE OF IONTOPHORESIS ON THE PERMEABILITY OF THE EXCISED CORNEA

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**I**ONTOPHORESIS of therapeutic agents capable of ionization has been shown to give high intraocular concentrations of these substances. Since the epithelium of the excised cornea not only is virtually impermeable to electrolytes<sup>1</sup> but also possesses a high degree of electrical resistance,<sup>2</sup> the undamaged cornea would seem to be unsuited to the iontophoretic transfer of ions.

The appearance of a transient epithelial haze after the use of iontophoresis has been noted by several investigators.<sup>3</sup> This is usually reported as clearing within a few hours, but in 1 case a 4 mm. nebula persisted three weeks after treatment.<sup>3a</sup> These observations considered with the finding that damage to the corneal epithelium increases its permeability to penicillin<sup>4</sup> lead one to suspect that the reported efficacy of iontophoresis may be due to epithelial injury. Von Sallmann clearly demonstrated by in vivo experiments that the iontophoretic transfer of penicillin into and through the corneas of rabbits was accomplished by a depressant effect of current flow on the barrier properties of the epithelium, by ionic transfer and, to a slight degree, by diffusion.<sup>5</sup>

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This paper has been accepted in completion of requirements for the Diploma in Ophthalmology of McGill University, Montreal, Canada

1. Cogan, D. G., and Kinsey, V. E.: The Cornea: I. Transfer of Water and Sodium Chloride by Osmosis and Diffusion Through the Excised Cornea, *Arch. Ophth.* **27**:466-476 (March) 1942.

2. Holt, M., and Cogan, D. G.: The Cornea: VIII. Permeability of Excised Cornea to Ions, as Determined by Measurements of Impedance, *Arch. Ophth.* **35**:292-298 (March) 1946.

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4. Wright and Stuart-Harris.<sup>3a</sup> Leopold, I. H., and Lamotte, W. O.: Penetration of Penicillin in Rabbit Eyes with Normal, Inflamed and Abraded Corneas, *Arch. Ophth.* **33**:43-46 (Jan.) 1945.

5. von Sallmann, L.: Controversial Points in Ocular Penicillin Therapy, *Tr. Am. Ophth. Soc.* **45**:570-636, 1947.

At the suggestion of Dr. David Cogan, director of the Howe Laboratory of Ophthalmology, the following investigation was undertaken to determine whether the procedure of iontophoresis is capable per se of altering the barrier properties of the excised cornea. This tissue is especially suitable for such studies, as Cogan and Kinsey have pointed out,<sup>1</sup> because of its maintained functional integrity after the death of the animal.

#### PROCEDURE

The permeability of the excised beef cornea was studied with and without iontophoresis. The procedure, modeled after that of Cogan, Hirsch and Kinsey,<sup>6</sup> consisted of tying excised corneas over the ends of glass tubes and placing within the tubes solutions of test substances. The lower, cornea-bearing ends of the tubes were then immersed in solutions initially free of test substances. In this manner, the penetrability of a test agent could be determined after any given time by assay of the material in the lower solution.

The tubes employed were made from Pyrex test tubes with inside diameters of 9 mm., which were converted into open tubes by removal of the rounded bottoms. The cross sectional area of these tubes was approximately 75 sq. mm.

Three kinds of test substances were selected for study: a cation, magnesium; an anion, chloride, and an essentially nondissociative substance, levulose. Magnesium was in the form of magnesium sulfate, and chloride, of sodium chloride.

The volume of the solutions containing the test substances was 2 cc. for the chloride and levulose investigations and 3 cc. for the magnesium studies. The volume of the solution in the container in which the cornea was immersed was 5 cc.

Determination of magnesium and levulose was performed colorimetrically, using the methods of Gillam<sup>7</sup> and Corcoran and Page,<sup>8</sup> respectively. Chloride was determined by titration with mercuric nitrate, as outlined by Schales and Schales.<sup>9</sup> The results for chloride determinations were corrected for blanks obtained from similar experiments when no additional chloride was present in the tubes. Similar blanks for levulose and magnesium gave zero readings.

Beef corneas from freshly killed animals were excised whole or after the removal of the epithelium in certain instances. These corneas were tied securely over the flared ends of the test tubes with the outer, or epithelial, side toward the lumen. It has been shown that it is difficult to obtain whole corneas without some damage to the endothelium.<sup>10</sup> Accordingly, to eliminate a possible

6. Cogan, D. G.; Hirsch, E. O., and Kinsey, V. E.: The Cornea: VI. Permeability Characteristics of Excised Cornea, *Arch Ophth.* **31**:408-412 (May) 1944.

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9. Schales, O., and Schales, S.: A Simple and Accurate Method for the Determination of Chloride in Biological Fluids, *J. Biol. Chem.* **140**: 879-884, 1941.

10. Cogan and Kinsey.<sup>1</sup> Leber, T.: Studien über den Flüssigkeitwechsel im Auge, *Arch. f. Ophth.* (pt. 2) **19**:87-186, 1873.



variable of mechanical endothelial damage, the endothelium was removed completely in all instances by rubbing this surface with a cloth.

Preliminary experiments with iontophoresis in unbuffered solutions revealed decided shifts in  $p_H$  values, presumably due to electrolysis of the sodium chloride derived from the cornea. To eliminate any effect of strongly acid or alkaline solutions on epithelial permeability, all solutions were therefore buffered. The  $p_H$  was adjusted initially to approximately 7.0 for the chloride and levulose investigations, and 7.6 for magnesium determinations. Two-tenths molar phosphate buffer solution was used for the chloride and levulose studies, and one-tenth molar barbital-hydrochloric acid buffer solution for the magnesium studies. These buffers limited the shift in hydrogen ion concentration to 1.0 or less  $p_H$  units. Direct observation during iontophoresis when colorimetric indicators were in the solutions showed no evidence of localized changes in  $p_H$  at the corneal surfaces.

The corneas which were subjected to iontophoresis were stationed in groups of six with platinum wire electrodes so placed that the corneas were in electrical series. This arrangement insured that each cornea was subjected to the same current. Care was taken that the electrodes were not in direct contact with the corneal surfaces. Strength of current was set arbitrarily at 2

TABLE 1.—*Transfer Through Corneas With and Without Epithelium  
(No Iontophoresis)*

Substance	Epithelium Intact	Epithelium Removed
Magnesium.....	0.00 mg.	0.49 mg.
Chloride.....	0.20 mg.	8.5 mg.
Levulose.....	0.07 mg.	3.7 mg.

milliamperes in all instances and was derived from a 110 volt direct current line, with 29,000 ohms of fixed resistance, 25,000 ohms of variable resistance and a milliammeter interposed. The standard period of iontophoresis was sixty minutes, an interval which permitted reasonably accurate quantitative estimation of the test materials.

The barrier properties of the epithelium to the test substances were determined (a) before iontophoresis, (b) during iontophoresis and (c) after iontophoresis, and a minimum of 6 corneas was used for each determination. All results are written as averages.

## RESULTS

*Before Iontophoresis.*—Table 1 shows the amounts of test substances which passed through corneas with intact epithelium and the amounts which passed through corneas from which the epithelium had been removed. In these experiments, the test substances were present for sixty minutes in 5 per cent solution, and no iontophoresis was employed at any time.

*During Iontophoresis.*—Table 2 shows the amounts of test substances which passed through corneas during sixty minutes of iontophoresis when the anode was on the epithelial side. It also shows the amounts passing through a similar number of control corneas tested simultaneously but not subjected to iontophoresis. The latter group

is analogous to that shown in column 1 of table 1. Test substances were again present in 5 per cent solution, and the corneal epithelium was present in all cases.

Table 3 shows the results obtained in a similar experiment but with current polarity reversed for the period of iontophoresis.

TABLE 2.—*Transfer Through Intact Cornea With and Without Iontophoresis (Anode on Epithelial Side)*

Substance	With Iontophoresis	Without Iontophoresis
Magnesium.....	0.19 mg.	0.00 mg.
Chloride.....	0.00 mg.	0.16 mg.
Levulose.....	0.74 mg.	0.05 mg.

TABLE 3.—*Transfer Through Intact Cornea With and Without Iontophoresis (Cathode on Epithelial Side)*

Substance	With Iontophoresis	Without Iontophoresis
Magnesium.....	0.00 mg.	0.00 mg.
Chloride.....	1.6 mg.	0.4 mg.
Levulose.....	0.02 mg.	0.05 mg.

TABLE 4.—*Transfer Through Intact Cornea with Iontophoresis Preceding Introduction of Test Substance (Anode on Epithelial Side) and Also Through Intact Cornea Without Iontophoresis*

Substance	With Iontophoresis	Without Iontophoresis
Magnesium.....	0.02 mg.	0.00 mg.
Chloride.....	0.57 mg.	0.24 mg.
Levulose.....	0.26 mg.	0.04 mg.

TABLE 5.—*Transfer Through Intact Cornea with Iontophoresis Preceding Introduction of Test Substance (Cathode on Epithelial Side) and Also Through Intact Cornea Without Iontophoresis*

Substance	With Iontophoresis	Without Iontophoresis
Magnesium.....	0.04 mg.	0.00 mg.
Chloride.....	0.56 mg.	0.26 mg.
Levulose.....	0.35 mg.	0.09 mg.

*After Iontophoresis.*—Table 4 shows the amounts of test substances which passed through corneas when iontophoresis preceded the introduction of the substances. In the experiments which are represented in this table, the anode was on the epithelial side of the cornea. Corneas were first subjected to iontophoresis with only buffer solutions on each side of the corneas. After the period of iontophoresis, sufficient test substance was added to the solution in the tube to give a final concentration of 5 per cent solution of that substance. This solution

was allowed to remain above the corneal epithelium for sixty minutes, without iontophoresis. A similar number of control corneas were treated identically except that they were not subjected to iontophoresis at any time.

Table 5 shows the results obtained in a similar experiment but with current polarity reversed for the period of iontophoresis.

Gross examination showed that all corneas subjected to iontophoresis had a diffuse epithelial haze after the procedure. It is interesting to note, however, that when these corneas were sectioned and stained the histologic counterpart of the epithelial haze was not capable of identification.

#### COMMENT

The results of experiments demonstrating permeability with and without the corneal epithelium (table 1) accord with previous observations which showed that the epithelium of the excised cornea is an effective barrier to substances of the nature of the test agents employed.

With iontophoresis in the presence of these substances, the penetration of magnesium and chloride ions through the cornea increased in a manner predictable on the basis of electrical attractions. Thus, the anions passed through the cornea toward the anode and the cations toward the cathode.

It is noteworthy that levulose, having  $p_K$ 's of 11.68 and 13.24, penetrated the cornea to a much greater degree when the anode was on the epithelial side than when the polarity was reversed. No explanation for this phenomenon is apparent.

In the third group of experiments (tables 4 and 5), in which iontophoresis preceded the introduction of the test substances, it was observed that the penetration of these substances was greater than penetration through control corneas not subjected to iontophoresis. Moreover, the penetration was greater when the iontophoresis, with polarity favoring in the instances of magnesium and chloride, was performed in the presence of the test substances than when it was performed before the addition of these substances.

On the basis of these findings, it seems reasonable to conclude that the barrier properties of the epithelium are impaired by the iontophoretic procedure. This change in permeability does not appear to depend on the changes in the hydrogen ion concentration in the buffered solutions employed. The impaired permeability thus would seem not only to permit the ions to move by diffusional processes due to their kinetic motion, but, in the presence of continued iontophoresis, to enable them to cross, at an accelerated pace, a previously nonconducting barrier. This barrier, in the absence of damage, is presumably resistant to the passage of ions, even with the aid of an iontophoretic current.

SUMMARY AND CONCLUSION

Iontophoresis increases the permeability of the epithelium of the excised cornea to magnesium, chloride and levulose.

It is concluded that this alteration in epithelial permeability is of major importance in obtaining the high intraocular levels which have been achieved by iontophoresis.

The staff members of the Howe Laboratory of Ophthalmology gave assistance and guidance in the execution of this work.

280 Queen's Avenue.

## TRACHOMA IN MISSOURI

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### HISTORICAL REVIEW

TRACHOMA is one of the oldest diseases known to man. Well known since Biblical times, it is still one of the greatest causes of blindness in the world. Among the ancient Romans and Greeks, such famous men as Aetius, Paulus Aeginetus, Alexander, Trailaus, Horace and Cicero were said to have been victims. It was known in ancient Egypt, and from the evidence of papyri and of crude instruments used for grattage and for trichiasis, one can assume knowledge of its ravages back to the nineteenth century B. C. India and Egypt are recognized as the "cradles of trachoma." It was known in ancient Greece, as is evidenced in the writings of Hippocrates, in the fifth century B. C. In 14 A. D. Celsus gave a good clinical description of the roughness of the lids and treatment by rubbing and scarification. Galen (131-201 A. D.), who practiced in Asia Minor, as well as in Egypt and Rome, mentioned various remedies for trachoma in numerous places in his writings. The Roman classical writers, including Pliny (23-79 A. D.), Marcellus (380 A. D.) and Cassius (447 A. D.), were evidently acquainted with its clinical manifestations. In medieval manuals, Greek and Arab surgeons gave lucid descriptions of its natural history and became adept at dealing with it. Shakespeare probably makes reference to this disease when he quotes Lancelot as saying that his father "was more blind than sand blind, he was gravel blind."

From time immemorial, trachoma has existed in Europe as an endemic disease, having been imported from its natural habitat in the Middle East by crusaders returning from Palestine. However, it was Napoleon's army that was deemed responsible for the general spread of the disease. When Napoleon invaded Egypt (1798), so many of his troops became infected with a purulent ocular disease that he was forced to return to the European continent. The disease became endemic in Europe and invaded England. One historian ascribes the loss of the battle of Waterloo to the prevalence of trachoma among the French troops. Trachoma was also known at that time as military

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From the Missouri Trachoma Hospital.

Read before the St. Louis Ophthalmic Society, April 2, 1948.

ophthalmia, and it spread rapidly throughout Europe, with devastating results, via the armies that overran the Continent during that period (1801-1820). The civilian population became infected in the wake of the military. When troops were disbanded and returned to their homes, they spread trachoma among their families.

In southern Europe, trachoma spread gradually over practically all of the continent and is still prevalent in southern European countries. England at one time had a very high percentage of trachoma, but the government established schools in which all children with trachoma were compelled to enter and remain until the disease was completely arrested. By this method, trachoma in England has been almost completely eradicated. At the present time it is epidemic in Egypt, China, Japan, India, Palestine, Iraq, Iran, North Africa and Russia. It is prevalent in Egypt in over 90 per cent of the population and is known there as Egyptian ophthalmia. In the United States, it is endemic in Missouri, Tennessee, Kentucky, Arkansas, Oklahoma, southern Illinois and West Virginia. Sporadic cases have been found in many other states.

To the best of our knowledge, trachoma was introduced into the United States during Colonial days by the early settlers from England and the Continent. Later, as a result of the increased prevalence throughout Europe following the Napoleonic wars, infection in America became more widespread with the influx of settlers from the British Isles. Duke-Elder<sup>1</sup> stated that trachoma in England is an alien disease, imported, propagated and passed to the native population by aliens. This may be a true statement, but it should be noted that the early English settlers were responsible to a large extent for bringing the infection to America and spreading it westward from the coastal settlements.

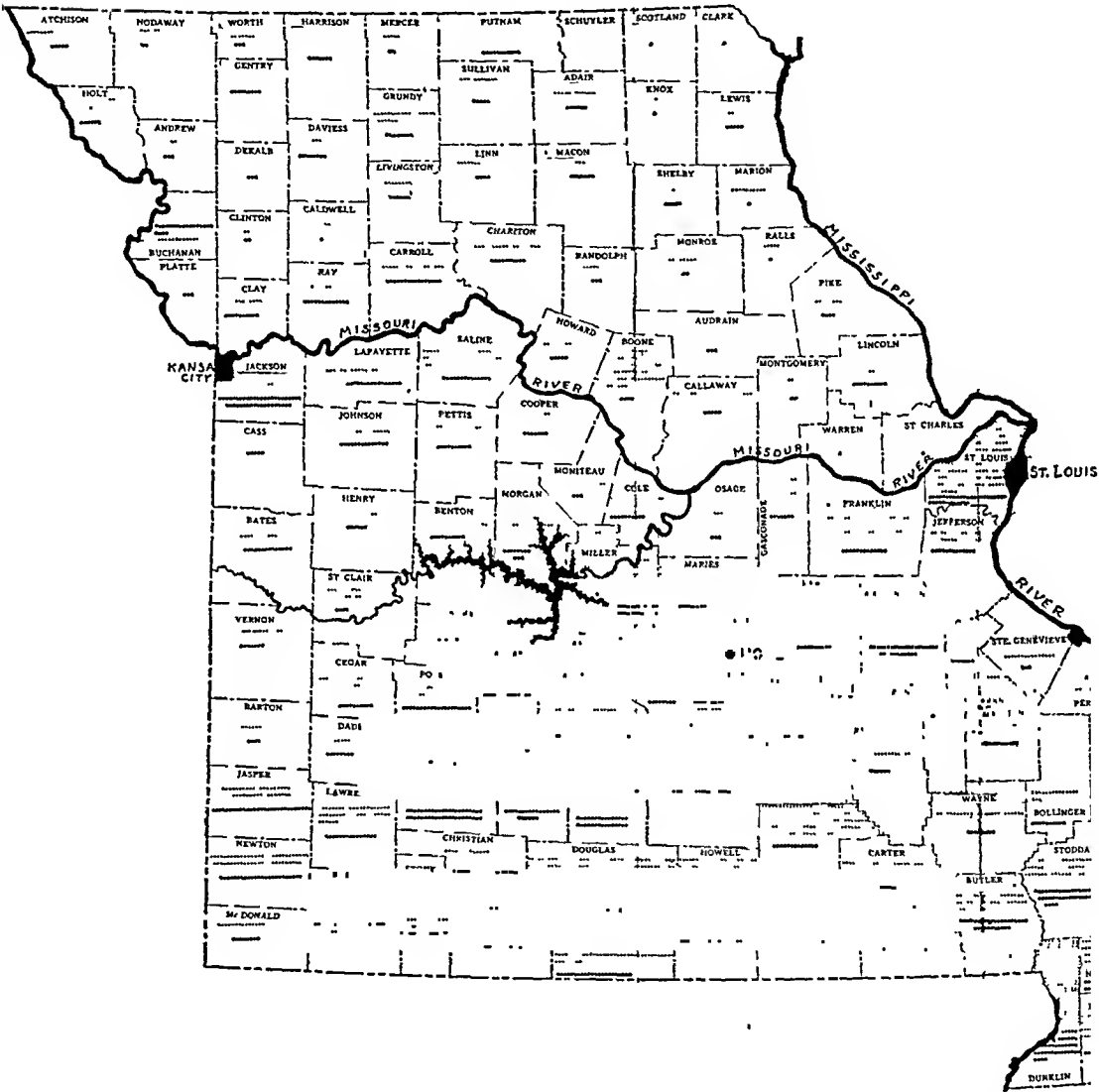
Trachoma was found first among the mountaineers of Tennessee, Kentucky and West Virginia. As emigration moved westward, these mountaineers carried their infection with them and spread it among the settlements. The southern half of Missouri and the northern half of Arkansas were settled to a great extent by immigrants from Tennessee and Kentucky. Although the most widespread infection is in the counties south of the Missouri River, there is not a county in the state that does not have a certain amount of trachoma (figure), spread by migratory laborers. During the recent war years, migration of families within the state and from state to state has tended to disseminate the disease.

Most of the Indian tribes of the United States are infected with trachoma, the percentage varying from 1 to 20. Whether or not trachoma was present among the Indians at the time of Columbus'

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1. Duke-Elder, S.: *Text-Book of Ophthalmology*, C. V. Mosby Company, 1946, vol. 2, pp. 1595-1596.

discovery is not accurately known. Fox,<sup>2</sup> after consulting more than thirty authoritative Indian works, as well as having personal communications with missionaries and other competent observers, reported that from time to time there have occurred among Indians pronounced epidemics of an ocular disease, epidemics that spread with great rapidity through the tribes and then subsided. He made reference to a kind



Distribution by counties (Missouri) of patients hospitalized at Rolla (total to 1948, 6,649) and of pensioners blind from trachoma (total to 1945, 1,259).

The former are represented by dots; the latter, by asterisks.

of grattage performed by the medicine men of several of the tribes, in which they used an improvised scraping instrument, made by sharpening one edge of a reed.

2. Fox, L. W.: The Trachoma Problem Among the North American Indians, J. A. M. A. 86:404 (Feb. 6) 1926.

In 1897 immigrants with trachoma were debarred from entering the United States. This has been largely efficacious in preventing the entry of foreign sources of infection. After World War II the American soldiers who returned from overseas duty were given rigid ophthalmologic examinations on discharge from the service, so that little foreign infection has been added to the population. The high standard of sanitation among the American armed forces has also been a factor in keeping the spread of this infection at a minimum.

Today, trachoma is probably the most widespread infectious disease of the eyes in the world, and is responsible for a greater percentage of blindness than any other one disease of the eye.

#### THE MISSOURI TRACHOMA HOSPITAL

The Missouri Trachoma Hospital is a state-owned and state-managed institution, having for its main purpose the treatment and eradication of trachoma within the state. The initial program was inaugurated by the United States Public Health Service, the facilities being available to victims of trachoma from adjoining states.

In the early twenties, the service began to concentrate in the Ozark region of southern Missouri, although still under federal management.<sup>3</sup> A mobile railroad car was supplied by the St. Louis-San Francisco Railroad Company for the purpose of housing and transporting the complete equipment and personnel of the trachoma service group. This car ran over the regular company tracks and contacted many towns throughout the state. It contained a complete clinic for registering and examining patients and for treating them on the spot. In many cases the necessary surgical treatment was performed in an operating room within the car.

Although this method of service covered a wide area, it lacked many of the advantages of being located in a permanent place, particularly with reference to hospitalization of patients with active medical and surgical trachoma. In 1923 the trachoma service came to Rolla and established itself in a wooden frame house on Elm Street. This was the first permanent location in Missouri. The frame dwelling served as an outpatient clinic and hospital and also provided quarters for the medical and other personnel. Patients with active and complicated disease were admitted and were kept under observation and treatment until their condition was improved or the process arrested. Surgical patients were encouraged to remain after operation until well healed. Experience had shown that patients with trachoma prematurely discharged after operation tended to have recurrences.

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3. The service was under the supervision of Dr. John McMullen, United States Public Health Service.



Many learned of the nature of the hospital, and letters and inquiries began to reach the office in regard to the type of service offered and the method of entering the hospital. Thus, the permanent nucleus for the present Trachoma Hospital was established.

As the years passed, the reputation of the hospital spread, and the people throughout the state began to associate Rolla with the trachoma service. During the early thirties, the ophthalmologists of St. Louis and Kansas City took an active interest in the little hospital at Rolla, and many visited it. These men encouraged the work that was being done and spread the word among their colleagues.

In 1934 the United States Public Health Service relinquished control of the Trachoma Hospital to the state of Missouri. Since that time the Missouri State Division of Health has supervised the service, its policies and its public relations.

As more and more citizens of the state became aware of the hospital and its program, and learned of and used its services, a need for a greater and more modern institution was felt. Therefore, in 1939, a new site was chosen at the outskirts of Rolla, and a modern concrete building was erected, with a patient capacity of fifty-five beds and quarters for four nurses. The main building includes administrative offices, dining rooms, a large modern operating room and sterilization room and additional space for laboratory facilities and conference rooms. A craft shop and playground have recently been provided for recreational activities. In addition to the regular hospital facilities, there is an outpatient service clinic, which cares for the needs of patients arriving from day to day for examination and diagnosis. Patients whose ocular conditions are not severe enough to warrant hospitalization are given eye drops for treatment at home and advised to return for reexamination at a later date. The patients with a severer condition are admitted to the hospital for intensive medical or surgical care. Bed and board, medical care and laundry are all furnished free; only transportation to and from the hospital is not provided. There is no restriction as to age, sex or economic status.

As a part of the general program for the eradication of trachoma within the state, field clinics are held at various county centers. These are primarily diagnostic and consultative. Some treatment, in the way of drops for home use, is dispensed. Newly found patients with active trachoma, as well as old patients who have had recurrences, are encouraged to enter the hospital for intensive treatment.

In addition to the necessary medical and surgical treatment of the eyes, the general welfare of the patient is not neglected. The hospitalized patient is given a well balanced and highly nourishing diet, supplemented with vitamin therapy when indicated. By precept and example, the patient is taught proper sanitary and hygienic living, and personal habits of cleanliness are emphasized. Thus, a majority of the patients

with arrested disease are returned to their homes in improved general health, with a higher regard for personal welfare and with instructions concerning the means of avoiding reinfection.

#### TRACHOMA

The word trachoma is taken from the Greek, *τράχωμα*, and its meaning is "rough." The name is well chosen, as the infection is primarily an inflammation of the tarsal conjunctiva of the eyelids, causing a roughened appearance of this membrane. It is also called popularly "granulated lids." It is a chronic, nonsuppurative disease of the palpebral, bulbar and corneal conjunctivas. The disease is not of bacterial origin; in the light of present knowledge, it is believed to be caused by a virus, or minute elementary (inclusion) bodies too small to be visualized by ordinary microscopes. Pus, when present, is due to a secondary invader. Infection may occur from transfer of the secretion by means of towels, washcloths, bed linen, pillows, clothing, handkerchiefs or other articles which may be brought into contact with the eyes, or by personal contact. Most important is the factor of intimate contact with a trachoma-infected person. The infectivity of trachoma is not high. It is the constant, intimate exposure over a period of weeks or months that accounts for its spread from one person to another. For this reason, families or groups living in close contact will more readily acquire the disease. Trachoma is not readily acquired by handling door knobs, pencils, eating utensils or institutional fixtures, although contact with such contaminated articles daily may enhance possibility of infection.

Because of overcrowding, trachoma is found more frequently among poor families. Their homes consist of rude dwellings. As a rule, the water supply is limited, being obtained either from a dilapidated well or a spring at some distance from the dwelling. Linen supplies and toilet articles in such homes are very limited; for instance, the family towel is commonly used by all members of the household. It is also usual for such families to have a common washbowl, in which all members wash their faces and hands, without changing the water.

Although the poor are more likely to acquire the disease, for the reasons just stated, it may also attack persons of education and higher financial standing. For example, during recent years, my associates and I have had among our patients at the hospital a doctor's son, a lawyer, several engineers, postal clerks, several clergymen, many business men and college students.

At present, trachoma is essentially a rural disease in Missouri. It is becoming increasingly rare in large cities. The vast majority of patients who attend the Trachoma Hospital come from communities with a population of less than 1,000, and a great many come from small hamlets, or even from thinly settled regions situated miles from a

highway. Only about 10 to 20 per cent of the patient census is made up of urban residents. Mossman<sup>4</sup> attributed the low rate in cities to the easy accessibility of oculists and to better living conditions.

Certain races are more susceptible than others; yet no one is immune except the Negro. Full-blooded Negroes do not acquire this disease, but persons of diluted racial strains may become infected. When the latter acquire trachoma, the course of the disease is always mild. By contrast, from my personal observation, it can be said that among the native Nordic white persons of Missouri the disease manifests a striking virulence and produces highly distressing symptoms, and it results frequently in irreparable complications. The conjunctivitis, when fully developed, is acute, painful and depressing, with intense photophobia and swollen lids. The patient presents a truly pitiable picture and is usually immobilized by his affliction, necessitating hospital treatment. The advanced complications of corneal ulceration, with perforation, severe blepharospasm, intense photophobia (even in a shaded room), edema of the conjunctiva and a proliferative pannus with cicatrization and symblepharon—these form the picture commonly seen in persons with advanced trachoma in Missouri.

On the other hand, trachoma among the inhabitants of the Middle East does not exhibit such virulence or produce such a devastating picture. Wilson<sup>5</sup> stated that trachoma among Egyptians tends toward spontaneous cure more frequently than among Europeans. He observed further that some of the Egyptians suffer little from this disease and that the lesions are mild, in contrast to the severity of the lesions among Europeans. Wilson stated the belief that this is not due to attenuation of the virus, because when Egyptian trachoma passes to the conjunctiva of an Englishman it produces severe, distressing symptoms and much suffering.

In my opinion, some degree of racial immunity exists among the French and Italian descendants living in Missouri. Many of these people reside in the trachoma areas of Missouri and are exposed to this infection under the same conditions as are other native white persons; yet when such patients are infected with trachoma, they exhibit only the milder symptoms, with moderate scarring of the eyelids, little or no involvement of the cornea and insignificant pannus that involves little or no visual loss. Although other factors may be concerned, this is undoubtedly due to inherent racial immunity. For example, the Italians of Rosati (a community producing wine and grapes, 100 miles [160 kilometers] southwest of St. Louis) live together in a settlement

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4. Mossman, P. D.: Present Status of the Trachoma Situation in the United States, *Eye, Ear, Nose & Throat Monthly* 9:430-435 (Nov.) 1930.

5. Wilson, R. P.: Trachoma: A Selection of Personal Observations and Experiences, *Giza Memorial Ophthalmic Laboratory 14th Report, 1939-1944*, pp. 24-25.

of their own, in a county (Phelps) where the incidence of trachoma is high (figure). These people attend the same schools, have commerce with neighboring people and intermarry freely with the non-Latin races of their communities, so that the exposure factor and standards of living are comparable to those of the surrounding peoples. The same is true of French descendants in Washington County (Potosi), Ste. Genevieve County and the Cape Girardeau area, where the incidence of trachoma is high. In contrast, the Anglican and Germanic white descendants living in the same areas are far more likely to have the disease in its severest forms.

Green<sup>6</sup> suggested that the heavily pigmented eye may have more inherent immunity to the trachoma virus than the more lightly pigmented eye. This concept would explain the reason that trachoma exhibits such virulence and destruction of tissue in the Nordic European, and that the disease provokes a milder response among Southern Europeans, Mediterranean peoples and the Indians of North America and of Asia. This, furthermore, would account for the apparent immunity of the Negro. It should be stated, however, that in a large percentage of native Missourians of both Nordic and non-Nordic extraction having dark brown irises and deep pigmentation some of the worst ravages of this disease develop.

In trachoma there is practically no acquired immunity. Once a patient has had the disease and has then recovered, he may still suffer another attack at some later date. The second or third recurrence may be even worse than the original attack, and may occur even after a fairly long period of quiescence. Patients who have had few and mild complications and who have escaped without serious damage to vision seem to be more liable to recurrences. Patients with stubborn disease with many complications which finally become arrested are, in my opinion, less likely to have recurrences. It is possible, therefore, that some individually acquired immunity may develop, although, unfortunately, only after the disease has first taken its toll on the eye of the sufferer.

Climatic conditions are predisposing factors to some extent, the southern or warm climates being the localities where trachoma is most prevalent. Arid lands, especially where the atmosphere is filled with dust and sand, favor the development of this disease. Thus, trachoma is highly prevalent in the southeast ("boot heel") corner of Missouri. Although predominant in the Ozark mountains, trachoma is prevalent to a considerable extent in the lowlands and in flat country. For example, one may note that trachoma is widespread in the Egyptian delta, in the Middle East, in the lowlands of the Netherlands and Belgium (following the Napoleonic wars) and, in the United States,

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6. Green, John: Personal communication to the author.

in southern Illinois and in southeast Missouri (figure). On the other hand, the high Tyrol and Alpine regions of Europe are relatively free of this infection. The Prague Clinic study in 1921, after World War I, revealed that the rich agricultural district of the Elbe River was favorable to the spread of the infection, while the mountainous districts were remarkably free. Lack of sanitary conditions among the agricultural population was given as the chief factor favoring spread of the disease.

Food and vitamins<sup>7</sup> do not seem to play any important role in this disease. Some writers have stated the belief that inadequate diet and avitaminosis were contributory factors. Stucky,<sup>8</sup> who made a great contribution to the prevention of trachoma in Kentucky, was an ardent supporter of this thesis. At present this concept must be regarded as unproved.

The incidence of trachoma is not influenced by age, as the disease occurs at all ages. The greatest number of hospitalizations are of persons between 15 and 35 years of age, the next, of persons between 35 and 60 years, and the fewest, of persons 15 years old or under. These groupings conform to the occurrence of the disease in active form among patients seen in the field.

In Missouri, males are frequently affected more than females, in the ratio of about 2:1. Thus, the Trachoma Hospital was built to accommodate twice as many males as females, and this ratio between the sexes has been consistently maintained in the distribution of hospital patients. This cannot be explained by the women being more timid about submitting to an examination, since in our field and hospital clinics more females than males present themselves for examination. The reason is undoubtedly epidemiologic.

#### TREATMENT

Trachoma can be cured if treatment is begun in its early stages. Moderately advanced forms can often be arrested, but the patient may suffer a relapse. Advanced trachoma with scar formation and visual loss can be arrested and the eyes freed of symptoms, but rarely, if ever, is the sight restored. If the disease is left to progress year after year untreated, it generally leads to blindness.

In most cases the disease responds well to treatment<sup>9</sup> with sulfonamide drugs. In recent years, the tendency has been toward mild, or

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7. Rice, C. E.; Sory, R.; Smith, J. E.; Faed, P. E., and Drake, A. A.: Effects of Diet and Vitamins on Trachoma, *Am. J. Ophth.* **17**:735 (Aug.) 1934.

8. Stucky, J. A.: Observations and Experiences with Trachoma in Eastern Kentucky, *Tr. Am. Acad. Ophth.* **35**:217-224, 1930; *Eye, Ear, Nose & Throat Monthly* **9**:455-457 (Dec.) 1930.

9. The subject of treatment is more fully discussed in a paper, "The Sulfonamide Drugs and Penicillin in Treatment of Trachoma," *Am. J. Ophth.*, to be published.

bland, treatment in preference to the older, harsh methods. Although of time honored use, copper sulfate and silver nitrate sticks, as well as solutions of these drugs, have been abandoned at the Missouri Trachoma Hospital in favor of milder remedies. Copper sulfate and silver nitrate are caustic, irritative to the conjunctiva and devitalizing to the infected tissues; furthermore, they add to the discomfort of the patient. Moreover, the continued use of silver preparations causes staining of the conjunctiva (argyrosis), and may even increase scar formation. In their stead, the sulfonamide drugs stand as first choice because of their relative mildness of action and their apparent specificity against the trachoma virus. In my opinion, at least, trachoma responds to treatment with the sulfonamide drugs more quickly and with least injury to the affected tissues than to use of any other drug previously used. Although Wilson<sup>10</sup> expressed disappointment with the results of treatment of Egyptian trachoma with sulfonamide drugs, it should be pointed out that he made use of the drugs only by oral administration, and not by local instillation into the conjunctival sac. In my opinion, use of the newer, highly soluble sulfonamide drugs in solutions instilled locally into the conjunctival sac at frequent intervals is the treatment of choice. The drops have proved to be a more effective means of treatment than the tablets when the latter are given alone by mouth. It is probable that a combined method of sulfa drops instilled locally and tablets given internally may yield the best therapeutic results.

At present our treatment of choice is (1) the administration internally of sulfadiazine or combisul<sup>®</sup><sup>11</sup> in 0.5 Gm. tablets, 4 to 8 tablets per day, the number depending on the patient's weight; (2) the local use of sodium sulfacetimide,<sup>12</sup> in 10 per cent solution, or of a similar sulfonamide compound, NU-445<sup>13</sup> (gantrisin<sup>®</sup>) in 10 per cent solution, instilled into the conjunctival sac every two hours during the daytime, and (3) the application of sodium sulfacetimide ointment (10 per cent) locally between the lids for overnight. Occasionally, when a patient does not respond well to the sulfonamide treatment, he may be put on a course of silver nitrate, 0.0125 per cent solution, instilled once daily in the morning, to be followed every two hours with zinc sulfate, 0.0125 per

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10. Wilson, R. P.: Trachoma: A Selection of Personal Observations and Experiences, Giza Memorial Ophthalmic Laboratory Publication, 14th Report, 1939-1944, p. 35-36; 13th Report, 1938, p. 98-99.

11. Combisul,<sup>®</sup> marketed by Schering Corporation, consists of a combination, in equal parts, of sulfadiazine, sulfathiazole and sulfamerazine.

12. Highly soluble sulfonamide compounds. Although soluble to a concentration of 30 per cent, the 10 per cent dilution was found to give optimum results in treatment of trachoma.

13. A new Hoffmann-LaRoche highly soluble sulfonamide compound not on the market, and now licensed only for experimental use. The drug is supplied in 0.5 Gm. tablets and in 10 per cent aqueous solution.

cent solution, throughout the day. This period of astringent treatment is carried out for one or two weeks, and the patient is then returned to the sulfonamide routine. Occasionally, silver nitrate 1 per cent solution, (never a stronger concentration) is applied with an applicator directly to the palpebral conjunctivas and deep into the upper and lower fornices, and immediately thereafter the conjunctival sac is flushed out with isotonic sodium chloride solution.

A new sulfonamide drug, still in its experimental stage and designated as NU-445<sup>13</sup> at this writing, has been used at the Trachoma Hospital, with highly satisfactory results. It is given in the form of tablets (0.5 Gm.) by mouth and also in the form of an ophthalmic solution (10 per cent, aqueous) for local instillation. Not only is it a highly soluble form of sulfonamide compound, but it has been found to be relatively free of toxic side effects.

These procedures have been found to be most beneficial, especially in cases of early and moderately advanced trachoma, with or without pannus. Late forms, with cicatrization, entropion and corneal ulceration, are also benefited but frequently require supplementary treatment with tetracaine (pontocaine®), atropine, heat, cautery and wet dressings. If uveitis has developed, typhoid and paratyphoid vaccines U. S. P., given intravenously, have been found useful.

Surgical treatment is also indicated in cases of entropion,<sup>14</sup> to correct the incurvation of the eyelids; in cases of trichiasis, electrolytic epilation is useful for destruction of individual hair follicles; exuberant conjunctival growths are best handled by grattage. The tear sac may become infected, requiring extirpation; deep infection of the globe (panophthalmitis) may call for enucleation.

Important in the management of trachoma is persistent and long-continued treatment, usually many months, or even a year. On the patient's discharge from the hospital, drops are provided for home use, with the injunction that he be regular and persistent in their use. As it is a common human failing to become careless when improvement is noted and subjective symptoms are relieved, some patients do not exercise the endurance to keep up a long course of treatment. Such persons often return to the hospital with a relapse, which is usually severer than the original condition.

#### DIFFERENTIAL DIAGNOSIS OF TRACHOMA

There are four types of conjunctivitis which show a close resemblance: trachoma, follicular conjunctivitis, inclusion blennorrhea (commonly called swimming pool conjunctivitis) and vernal conjunctivitis (vernal catarrh).

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14. Smith, J. E., and Siniscal, A. A.: Modified Ewing Operation for Cicatricial Entropion, *Am. J. Ophth.* **17**:382-389 (April) 1943.

*Trachoma*.—An early symptom of trachoma is the sensation of having a foreign body in the eye, accompanied with photophobia and lacrimation. The patient first complains of a stinging, burning sensation. If he lives on a farm, he often thinks he has a husk of wheat or a like object in his eye, but when the condition prevails he seeks help. The incubation period for trachoma is from two to three weeks, while the duration may be for life. Uncomplicated trachoma does not produce pus, which occurs only from a secondary infection.

The diagnosis is usually difficult during the early stages. There are five cardinal points to be borne in mind: (1) the presence of inclusion bodies; (2) papillary hypertrophy of the retrotarsal region of the lids, with softening of the tarsus; (3) vascularization of the cornea (pannus); (4) scarification of the conjunctiva, and (5) history of contact with a known infected person or of residence in a trachoma community.

The microscopic examination for Prowazek inclusion bodies should not be given too great importance. When the latter are found in a case of suspected trachoma, one may assume a positive and conclusive diagnosis, but failure to find these bodies does not necessarily rule out trachoma. As a rule, inclusion bodies diminish rapidly after the first several months after onset. Wilson<sup>15</sup> stated that inclusion bodies must be sought for at the right stage. In Egyptian trachoma he found that they rapidly decrease in number and that they are difficult to find after the disease is well established. Special training on the part of the laboratory technician is required for their detection; hence, a negative laboratory report should be taken with reservations. Consequently, more emphasis must be placed on the clinical signs, family history and contacts than on laboratory diagnosis in the individual case.

On everting the lid, one may find either the papillary or the granular type<sup>16</sup> of trachoma. Occasionally both types are present in the same lid. In the papillary type, the lids present a red, velvety or beefy appearance, caused by an increase in thickness of the surface of the hypertrophied conjunctiva. Often, a grayish or translucent cast is given to the palpebral conjunctiva. This papillary hypertrophy is not a distinctive characteristic of trachoma, as it may also be seen in cases of long-standing chronic catarrh, senile ectropion, encapsulated foreign body of the conjunctiva and other prolonged conjunctival inflammations. By contrast, the granular, or follicular, type is characterized by the presence of granulations (or follicles), which are really small lymph follicles formed by rounded aggregations of lymph corpuscles. These

15. Wilson,<sup>5</sup> pp. 16 and 26.

16. The older Fuchs classification is used here, for simplification, rather than the newer MacCallan, four stage classification.



are large, devoid of sharp outlines and deeply embedded in the conjunctival surface. As a rule, the follicles are more commonly distributed in the retrotarsal region of the upper lid. For this reason, it is highly important when one is making the examination to evert the eyelid over a suitable lid everter,<sup>17</sup> so that the retrotarsal fold can be exposed and viewed thoroughly from the nasal to the temporal angle.

It is my belief, based on observations over a number of years, that the granular type of trachoma is becoming less frequent in Missouri. In former times it was fairly common to see many patients with the florid, inflammatory granules in the everted upper and lower eyelids and cul-de-sacs. Such a picture is now rare in Missouri. Today, the trachoma commonly seen is the papillary type, with the smooth, velvety, grayish or purplish conjunctiva, devoid of follicles. The granular type of inflammation is still seen occasionally in children and young adults.

If the infection has prevailed for as long as three months, one should be able to detect small vessels encroaching on the cornea, coming from above; this vascular invasion is called a pannus. This finding is absolutely diagnostic of trachoma. Trachoma can occur, nevertheless, without the presence of pannus. I cannot agree with the statement that some degree of pannus must be present in every case of trachoma.<sup>18</sup> In many cases a most searching examination with the slit lamp and corneal microscope will fail to show any evidence of pannus, although other cardinal signs may be clearly apparent. The explanation can only be that, while in most cases the virus attacks the conjunctiva of the lids and the cornea concurrently, there are frequent instances in which the main force of the onslaught is concentrated either in the palpebral conjunctiva or in the corneal conjunctiva (i. e., epithelium).

A pannus is not secondary or merely incidental to the roughening of the upper eyelid, or to so-called "mechanical irritation" from the lid (e. g., pannus occurs in many cases with smooth eyelids); but it is due to a specific invasion of the cornea by the virus. The resulting vascularization follows as an inflammatory defense reaction by a normally avascular tissue against the virus attack.

A true pannus cannot be positively defined as such unless short twigs or downward sprouts are present along the vessels of the upper portion of the corneal limbus. The loops of blood vessels, or "festoons," seen encroaching on the cornea at the upper portion of the limbus are not to be interpreted as true pannus; there must be present small twigs or downsprouts which arise as off-shoots from the main plexus of

17. Siniscal, A. A.: Siniscal-Smith Lid Everter, *Am. J. Ophth.* **28**:198-200 (Feb.) 1945.

18. Duke-Elder<sup>1</sup>, p. 1609. Wilson, R. P.: Giza Memorial Ophthalmic Laboratory Publication, 1932, Vol. 7, p. 88.

vessels that form the circulus around the limbus. The small twigs seen in early cases may grow eventually to larger size and in time may cover the entire surface of the cornea (generalized pannus). A clear and concise summary of incipient pannus was given by Kuo<sup>19</sup> in his excellent paper on trachoma at the Chungking Army Hospital. Kuo laid much stress on the importance of incipient pannus and the general haziness of the lower cul-de-sac as important features in establishing an early diagnosis. With this view I heartily concur.

In the absence of pannus trachoma can be confused with vernal conjunctivitis, inclusion blennorrhea or folliculosis. In this case the diagnosis is rather difficult, and repeated observations may be necessary to establish a correct diagnosis. A history of contact (exposure) or of residence in a trachoma district is of value. In such circumstances the experienced observer will rely on other diagnostic features. For example, in trachoma hypertrophied conjunctiva tends to crack and bleed on eversion of the lid, and some of the larger follicles may rupture on pressure and extrude their gelatinous contents. Furthermore, the vessels of the upper cul-de-sac are partially or entirely covered by the overgrowth (hyperplasia) and cannot be seen. This point is of diagnostic importance in differentiating trachoma and follicular conjunctivitis, in which the vessels can easily be seen between the follicles. Another point to be borne in mind is the loss of rigidity of the tarsus; this is felt by the examiner's fingers in holding the lid when the upper lid is rolled back over a suitable lid evtor.

In the early, active stages, one will usually find the tarsus succulent and thickened; this condition, by subsequent degeneration, leads eventually to softening, cicatrization and deformation. Another important conjunctival sign is the general haziness of the lower cul-de-sac, especially at the margin of junction between the bulbar and the palpebral folds. It is seen early in the disease, frequently before pannus has developed. This is due to subconjunctival infiltration and may be present in the upper cul-de-sac to a lesser extent. Another diagnostic hint is the copious tearing that follows manipulation of the everted eyelids. The presence of white striae (cicatrices) in the retrotarsal fold is also an important diagnostic feature.

*Follicular Conjunctivitis.*—This condition is a follicular lymphoid hypertrophy of the conjunctiva found commonly in young adults, rarely beyond the age of 18 or 20. Without a secondary infection, the patient often does not complain of the condition. The follicles look like those of trachoma, but are smaller, more sharply limited, project farther above the conjunctival surface and occur most frequently in the lower

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19. Kuo, P. K.: Incipient Pannus in Early Diagnosis of Trachoma, *Am. J. Ophth.* 29:645-653. (June) 1946.

fornix. They are usually oval and arranged evenly in rows, like strings of pearls, whereas trachoma granules are round and rarely present such a regular arrangement. This disease does not lead to pannus, does not form scar tissue and usually heals spontaneously. Folliculosis does not attack the cornea, whereas as time does on trachoma attacks the cornea, causing pannus formation, ulcers and scar tissue, with subsequent loss of vision and even complete blindness.

*Inclusion Blennorrhoea (Paratrachoma; Swimming Pool Conjunctivitis).*—This condition is also a virus disease, directly contagious, relatively harmless and only rarely accompanied with corneal ulceration. It resembles very much acute, reddened, papillary trachoma, causing considerable lacrimation and photophobia; but, in addition, it is a purulent disease. It does not form a pannus or injure the cornea. Neither does it destroy the conjunctiva, though it may be followed by fine, superficial scars. So far no method of treatment has been found adequate, although recovery may be expected in from one to six months. It occurs in the newborn, as well as in children and adults. In infants it resembles a mild attack of ophthalmia neonatorum.

*Vernal Conjunctivitis.*—This condition is a trachoma-simulating disease, found as a rule in young adults. It is related to summer weather, but whether to heat or light is not known. Some investigators regard it as due to allergy. The presence of eosinophils in the secretion is an important differentiating point. Symptoms are in abeyance during cold weather but become worse on the approach of spring. The warmer the season, the greater the intensity of the symptoms. The disease recurs annually for years, when it finally disappears, leaving no trace. The clinical picture of the conjunctiva remains the same, summer and winter, except that during acute periods the conjunctiva appears more injected and the eyes become reddened and watery. Constant itching and photophobia are present. The appearance of the lid on eversion is that of "cobblestone" formation on the tarsus, due to the development and proliferation of conjunctival follicles. The resemblance to trachoma is striking. However, these follicles are hard and creamy white, somewhat like cartilage. At present little or nothing is known of its causation and treatment. Such patients can be made more comfortable by cold packs, collyria containing epinephrine and camphor water and irrigations. Commonly found during the period of adolescence, it tends to disappear in adult life.

Also to be considered in a differential diagnosis are Parinaud's conjunctivitis (leptotrichosis of the conjunctiva), some fungous infections (sporotrichosis and actinomycosis), tuberculous conjunctivitis (when follicular in type), syphilitic conjunctivitis (when granular in type), acute pneumococcic conjunctivitis (in some cases) and encapsulated

foreign body in the conjunctiva. In most of the aforementioned conditions there is present some degree of preauricular or cervical lymphadenopathy, whereas in trachoma, even when the infection is attended with common secondary invaders, there is never any degree of local lymphadenopathy.

#### CONCLUSION

Trachoma is still one of the principal factors in the causation of blindness in the state of Missouri. Until recently it was responsible for about 16 per cent of the total known cases of blindness, and for about \$250,000 per year in pensions for the blind. The incidence of trachoma in Missouri at present is on the decline. This is due to the work carried on by the Trachoma Hospital; to greater cooperation by patients, both during hospitalization and subsequently, and to earlier referral of patients by physicians and other agencies. Prior to 1926, according to the Blind Pension figures,<sup>20</sup> trachoma was responsible for 25.5 per cent of the cases of total blindness; from 1926 to 1935 it was responsible for only 14.4 per cent of the total blindness, and since 1935 and up to the present census figures (for 1944), for only 12.3 per cent of the total blindness. Comparable percentages for other causes of blindness in Missouri, revised to 1944, were as follows: glaucoma, 18; trauma, 12; cataract, 11, and syphilis, 8.6. However, it should be noted that these figures do not indicate rates of occurrence or of prevalence, because this roll covers only a portion of the total cases of blindness and is actually a selected list. At any rate, these figures offer proof of the effectiveness of the program for control of trachoma in the state of Missouri.

The control and eventual eradication of trachoma will depend on the discovery of all persons with trachoma and an ophthalmologic examination of all contacts and associates of persons with recognized trachoma; the treatment of infected persons at the hospital or home (depending on the severity of the infection), and, finally unremitting conformity to principles of personal and ocular hygiene on the part of the patient and his family. A rise in the economic status and general educational standards in the affected population will decidedly improve trends toward eradication of the disease in Missouri. Prevention through public health education is even more important than cure.

It is hoped that in time the disease will be entirely wiped out and that within the years to come it will be remembered only as an extinct clinical entity.

Missouri Trachoma Hospital.

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20. Statistics on Pensions for the Blind, from the Fifteenth Biennial Report, Missouri Commission for the Blind, 1943-1944.

## CONDITIONED CORNEAL VASCULARITY IN RIBOFLAVIN DEFICIENCY

Report of a Case

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IN 1940 Sydenstricker and his associates<sup>1</sup> published their observations on corneal vascularization in man, which was similar to that described previously by Bessey and Wolbach<sup>2</sup> in rats maintained on riboflavin-deficient diet. Since then a large number of papers on the subject have appeared, and the first enthusiastic response of confirmation soon made way to criticism and doubt; the latter trend, as happens frequently, shifted the general opinion far in the opposite direction, causing a number of workers to deny the existence of corneal vascularity as a result of ariboflavinosis in man. This negative attitude seems to have taken root to a certain extent in the collective mind of ophthalmologists.

Corneal vascularity caused by riboflavin deficiency is a clinical entity. It is probably true that it cannot be diagnosed by its morphologic aspect alone, although the appearance of regular, fine capillaries in the entire circumference of the cornea, which leave the limbic zone and pass centripetally into the clear cornea, is highly suggestive; if, in addition, three conditions are fulfilled—inadequate riboflavin intake, low riboflavin level of the blood or urine and response to treatment with riboflavin—there is no doubt as to the cause of the lesion.

The following case report is presented because any additional clinical observation on the relation of this lesion to riboflavin deficiency is worthy of attention if it establishes the validity of the concept first expressed by Bessey and Wolbach and by Sydenstricker and associates.

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From the Nutrition Clinic of the Department of Health of the City of New York, and the Special Eye Bank Clinic of the Manhattan Eye, Ear and Throat Hospital, New York.

1. Sydenstricker, V. P.; Sebrell, W. H.; Cleckley, H. M., and Kruse, H. D.: Ocular Manifestations of Ariboflavinosis: Progress Note, *J. A. M. A.* **114**:2437 (June 22) 1940.

2. Bessey, O. A., and Wolbach, S. B.: *J. Exper. Med.* **69**:1, 1939.

## REPORT OF CASE

E. A., a Greek veteran aged 38, was sent to this country by his government to seek cure for blindness, which he had contracted during army service. It was hoped that a corneal transplant might benefit him, and he came to the Special Eye Bank Clinic (Manhattan Eye, Ear and Throat Hospital), where Dr. R. Townley Paton referred him to the Nutrition Clinic of the Department of Health of the City of New York for study.

His vision had always been adequate prior to a shell blast injury received to his face and eyes in the early stages of the Greek-Italian war (1940). At this time he was taken prisoner by the Italians, and he spent the next five years in Italian and German prison camps. During this time his eyesight deteriorated steadily, and when he was finally returned to his country he was blind for all practical purposes.

When he was first seen at the Nutrition Clinic, he was a thin, dejected-looking man, who was hardly able to find his way in unfamiliar surroundings. His vision



Fig. 1.—Eyes before riboflavin therapy was started. *A*, right eye. *B*, left eye. Note the irregularity of the normally circular light reflex on the cornea, indicating the degree of unevenness of the epithelium.

was reduced to counting fingers at 2 feet (60 cm.). Both eyes showed injected conjunctivas, and photophobia was present. Both corneas showed diffuse opacities over the entire surface, chiefly in the superficial layers and the epithelium, with numerous engorged blood vessels entering the cornea from every point of the periphery, traversing it and freely communicating with each other. On the posterior surface of each cornea and the anterior surface of the lens, fine and gross particles of iris pigment could be discerned (fig. 1 *A* and *B*). There was dyssebacia of the face, but no glossitis or cheilosis.

A reconstruction of his diet during the war years showed that he had been on a diet seriously deficient in all members of the vitamin B complex, as well as in other vitamins. Riboflavin must have been practically absent from his diet. During all these years he had formed a faulty dietary pattern, and even now, with all restrictions removed, he consumed a diet inadequate in riboflavin. Examination of the urine for riboflavin at the Nutrition Clinic showed 70 micrograms in a four hour fasting specimen of 340 cc., a value indicating a low riboflavin intake.

Treatment was instituted with administration of 15 mg. of riboflavin by mouth. After one week, regression of the hyperemia of the corneal vessels could be observed, and the cutaneous lesion on the face was clearing. By the end of the third week the vessels in the cornea were considerably less noticeable. Some of the smaller ones could not be seen at all with the slit lamp, and the larger ones were less engorged and showed a reduction in caliber. Vision had improved to counting of fingers at 6 feet (180 cm.). The patient had gained 3 pounds (1.3 Kg.) and felt much better generally.

At the end of seven weeks, with no additional therapy, the majority of the vessels in the cornea had become invisible. Here and there, blood corpuscles could be seen in collapsed capillaries. In other capillaries very sluggish circulation was still evident. The opacities had receded considerably, and the patient counted fingers at 10 feet, or 3 meters (fig. 2). (He was myopic, and the visual acuity could still be improved with glasses.)

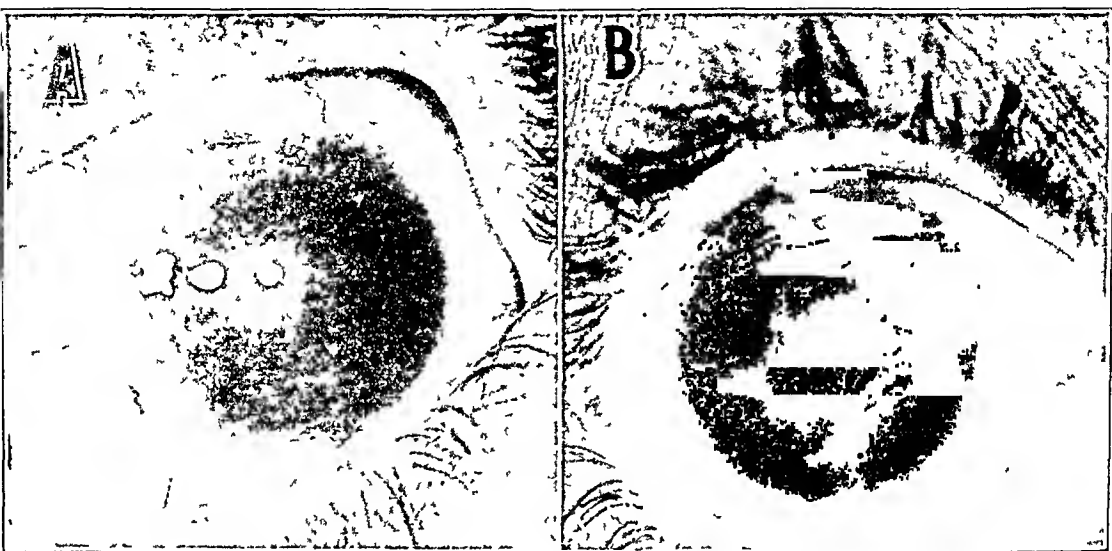


Fig. 2.—Eyes seven weeks later. *A*, right eye. *B*, left eye. Note that the light reflexes on the cornea are nearly circular, indicating that the epithelium is now almost normal.

There does not seem to be any reason to doubt that this case was one of true riboflavin deficiency. All the conditions are fulfilled: low riboflavin intake over a long period, low riboflavin level of the urine and prompt response to riboflavin therapy. Although a deficiency of all vitamins was probably present, only riboflavin was given as a therapeutic trial. It is hardly conceivable that pathologic changes of the degree described would recede spontaneously after having been present so many years. It can be concluded, then, that a long-standing deficiency of riboflavin in this patient's diet resulted in the specific lesions in his eyes, which were influenced most favorably by specific therapy.

This explanation, nevertheless, is not fully satisfactory. There must have been a very great number of people under nutritional handicaps similar to those of this patient during the war and the postwar years.

Yet, during the last few years, thousands of prisoners of war and inmates of concentration camps have been seen by a number of investigators, without any published reports indicating the presence of corneal vascularity in the degree seen in the present case. It appears, then, that the nutritional factor is not the sole explanation of the corneal vascularity in this case. An additional factor must have been present which, in combination with riboflavin deficiency, produced the clinical picture.

It has been shown by Bessey and Lowry<sup>3</sup> that the riboflavin concentration in the cornea of the rat must fall to less than 50 per cent of the normal before signs of corneal vascularity appear. Clinical investigations now under way seem to indicate that chronic riboflavin deficiency may produce corneal vascularization only if and when the cornea is exposed to a traumatic factor—be it accidental injury, surgical intervention, chronic mechanical or solar irritation or an allergic reaction. Landau and I<sup>4</sup> have argued the case for the last contingency in the instance of eczematous keratitis. The present case seems to support a position of major importance for trauma. During his army service the patient was subjected to bomb and shell blast on several occasions, and on one of these he received the full blast of an exploding shell in his face. The iris pigment scattered over the surfaces of the anterior chamber in both eyes was probably a result of this blunt injury. It seems justifiable to assume that the cornea was injured superficially and that the healing process was disturbed by the presence of a serious riboflavin deficiency.

Riboflavin is a prosthetic group of the yellow respiratory enzyme. Bessey and Wolbach<sup>2</sup> postulated that in its absence the disturbance of the respiratory processes in the avascular cornea is relieved by ingrowing vessels. Contrary to earlier opinions, the metabolism of the corneal epithelium is very active (Lowry and Bessey,<sup>5</sup> Robbie and associates<sup>6</sup>). An injured cornea requires more oxygen, consequently more respiratory enzyme, and therefore more riboflavin, than a healthy one. A degree of riboflavin deficiency which will remain subclinical under normal conditions will lead to corneal vascularization to relieve the respiratory deficit when pathologic conditions raise the corneal metabolism. It has been shown by Lowry and Bessey<sup>5</sup> that a prolonged deprivation of riboflavin leads to a fall in the riboflavin concentration in the cornea, causing a definite handicap to the healing of experimental lesions.

The corneal condition in the case presented here had remained static for many months. The patient had received the usual local treatment

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3. Bessey, O. A., and Lowry, O. H.: *J. Biol. Chem.* **155**:635, 1944.

4. Stern, H. J., and Landau, J.: *Am. J. Ophth.* **31**:1619 (Dec.) 1948.

5. Lowry, O. H., and Bessey, O. A.: *J. Nutrition* **30**:285, 1945.

6. Robbie, W. A.; Leinfelder, P. J., and Duane, T. D.: Cyanide Inhibition of Corneal Respiration, *Am. J. Ophth.* **30**:1381 (Nov.) 1947.



and had failed to show any response. The improvement under riboflavin therapy was too dramatic to be explained by anything but the contention offered here. It can safely be assumed that in this case a chronic deficiency of riboflavin had been "conditioned" (Jolliffe<sup>7</sup>) by superficial injuries to the cornea, the nutritional factor complicating their healing and causing the extensive opacities and vascularity which rendered him nearly blind. Specific therapy with the missing vitamin relieved this condition to such a degree that the patient acquired useful vision within a few weeks, thus obviating the necessity of corneal transplantation.

3 Hopper Street.

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7. Jolliffe, N.: Conditioned Malnutrition, J. A. M. A. **122**:299 (May 29) 1943.

## PERSONALITY PATTERNS IN OCULAR DISCOMFORT

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THE MOST frequent reason that patients seek the services of an ophthalmologist is their inability to use their eyes with comfort. As a rule, the patient with visual impairment does not come into a physician's office early but tends to procrastinate. The causes of ocular discomfort are many, but no attempt will be made to give a differential diagnosis of ocular discomfort here. Rather, I shall analyze observations on a group of patients with ocular discomfort other than that due to refractive errors, improperly made glasses or poorly adjusted glasses, as discussed by Veasey.<sup>1</sup> These patients form a distinct group whose complaints are real and whose symptoms cannot be relieved by merely treating the patient as a rigid optical apparatus, without regard for his personality, of which the ocular component is only a small part. If the physician but understands the personality patterns of these patients and if, after finding nothing abnormal on refraction and examination of the eyes, he takes the time to explain to them the possible root of their trouble and to give them the advice and reassurance that is necessary for the relief of their symptoms, he will have served them both as a physician and as an ophthalmologist.

In the study of ocular discomfort, it is of the utmost importance that a good history be obtained. The patient can usually give a rather definite time of onset of his symptoms. This is important, as the circumstances leading up to the evolution of his symptoms will usually give a clue to his reactions to various life situations, which must be understood before his complaints can be evaluated properly. At present, the ocular findings are usually pointed out after the symptoms have developed, but there is no way of knowing whether or not the condition was the same before the symptoms occurred. If it is accepted that a discomfort, an ache and a pain are various degrees of response to a stimulus, whether the stimulus is internal or external, psychogenic or organic, it is evident that the difference between the degrees of pain experienced by the same person depends on the degree of stimulation. However, the same degree of stimulation will not elicit the same degree of response

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1. Veasey, C. A.: The Dissatisfied Refraction Patient, *Am. J. Ophth.* **30**:1286-1293 (Oct.) 1947.

in different persons. It is not the stimulus itself, therefore, but the impact of the stimulus on a particular kind of person, that leads to symptoms of varying degrees.

#### ANALYSIS

*Period of Onset.*—Certain periods or situations in life will precipitate symptoms in persons of a particular type. Such situations are found between adolescence and middle age, the period of life in which the trial and stress of living show up the weak spots in a person's makeup. Symptoms of discomfort are rarely found in children because their emotive and mental attributes are not developed. Among such situations of stress are initiation into a job, a love affair, disappointment in vocational or financial affairs, pressure in establishing a place in the economic and social world, a death in the family, marriage, pregnancy, the menopause and incidents of adjustment in later life.

*Personality Characteristics of Groups.*—Such patients tend to be of a definite physical type. Women predominate over men, the ratio being about 8:2. In general, these patients are slenderly built. They dress neatly and well despite their actual economic station. Their habits and actions are orderly and well planned. This orderliness in their manner of dress and habits extends to their home and place of work, so that if anything is out of place they feel uneasy until order has been restored. They are endowed with a great deal of energy and "push" and appear tireless in their pursuit of the goal that "everything be just so." This inflexibility reflects itself in their actions and thinking. Such persons cannot delegate anything to be done by someone else, for they feel that no one can do it as well as they. This unyielding approach to life makes readjustment and compromise difficult, so that, rather than adapt themselves to a difficult situation in life, they resist and balk at the expense of their emotional system.

*Ocular Complaints.*—The ocular complaints of such patients are definite, although they vary in degree with the individual. He exhibits a characteristic quality of ocular sensitiveness or ocular consciousness which is above the average. There is a history of inability to read or sew, even for short periods, such activity usually being followed by a vague ache in the eyeball or along the supraorbital ridge, with later extension as the sensation of a tight, gripping band about the head. A great deal of exactness and detail is used in outlining the particular site of the ache and its ramifications. In such a description, one gets the impression that the vague ache has at times become almost unbearable and yet is stoically endured. Photosensitivity is rather characteristic, and the patient professes to have relief from the use of tinted or dark glasses. Even the glare of an ordinary light bulb causes such

a patient to change his sitting position in relation to the light, whereas other persons may not be disturbed by the same amount of light. The sensitiveness to light is a reflection of ciliary (cortical?) sensitivity, and the aching about the eyeball is a manifestation of ciliary spasm. Refraction with cycloplegia usually gives the patient relief from his symptoms for the time being. Spasm of the sphincters of the body is a common complaint of nervous, unduly irritable women, as has been pointed out by Alvares<sup>2</sup>; but why the sphincter of the eyes is a source of discomfort in one patient, and the sphincter of the pharynx, the pylorus or the anus in another, is difficult to explain. These sphincteral sites of physical disturbances are merely targets of a tensional state the expression of which in a particular sphincter depends on the emotional experiences and stability of the particular patient. That is to say, one's past experiences and associations have a definite influence on the manner in which one thinks and acts and feels (reacts).

*Experimental Work.*—Of extreme interest is the work of Cyriax,<sup>3</sup> who injected 0.1 cc. of a 4 per cent sodium chloride solution into the occipital insertions of the muscles of the neck, with the development of pain which ran forward like a band encircling the head and reached its maximum intensity in the temple and the supraorbital region. When the injection was made about 2 inches (5 cm.) below the occipital insertion, the pain was referred from the back of the head to the vertex. When the injection was made in the sternocleidomastoid muscle, the pain was referred to the temple. When the injection was made in the epicranial aponeurosis, the pain was referred to the eye, behind the eye and to the eyelids. Of particular importance is the fact that with each of these types of referred pain the patient interpreted the pain as being inside the head and that it bore no relation to its actual, superficial cause.

According to Wolff,<sup>4</sup> the most commonly encountered headaches are vascular, and these include migraine and tension headaches, which arise from sustained contraction of the muscles of the head and neck. Pain in the head, of whatever cause, may induce secondary contraction of the muscles of the head and neck, which when maintained becomes a source of pain in itself. Thus, a vicious cycle may be initiated, which, if unchecked, may cause a fixation of the condition, with resulting irreversible organic changes.

*Systemic Complaints.*—It is not uncommon for these patients to have many systemic complaints, in addition to those related to the head and neck. There is often a complaint of generalized muscular fatigue without

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2. Alvares, W. C.: Psychosomatic Medicine That Every Physician Should Know, J. A. M. A. **135**:704-708 (Nov. 15) 1947.

3. Cyriax, J.: Rheumatic Headache, Brit. M. J. **2**:1367-1368 (Dec. 31) 1938.

4. Wolff, H. G.: Headache and Other Head Pain, New York, Oxford University Press, 1948.

any tangible cause. Many such patients give the history of going to bed early to get rested, only to get up the next morning feeling just as tired as before. It is of interest to note the observation of Allan,<sup>5</sup> in a study of 300 patients with complaints of weakness and fatigue, that physical causes were found in only 20 per cent, whereas in 80 per cent the condition was attributable to a nervous condition. The patients are generally poor eaters and give a history of trying to gain weight but of being unable to do so. They all give a history of insomnia and are rather light sleepers. They tend to dream a great deal, and many plan their day's work in their insomnic state, so that they know just what they are to do the next day. This is in keeping with their determined perfectionistic, yet cautious, attitude toward life and their constant preoccupation with acquiring achievement and success. Although the personalities of these patients seem to fit a definite pattern, not all patients with the aforementioned characteristics complain of ocular discomfort. A person becomes what he is because of his individual accumulation of experiences and associations. Although many of these experiences are common to most people, it is the manner in which the individual person reacts to his emotional experiences that causes him to be what he is.

*Ocular Findings.*—These patients usually have a low refractive error. On refraction with cycloplegia, they will be found to be hypermetropic, and when a postcycloplegic refraction is done they prefer a minus lens. Their visual acuity is 20/20 without glasses, yet they prefer the sharp, dark outline that the minus lenses afford them. However, these lenses give only a temporary subjective relief, after which the patient feels better without them. The relation of abduction to adduction is not the 1:2 or 1:3 ratio which is usually given in textbooks. Analysis of the complaints of 100 patients in relation to the abduction-adduction ratio revealed that their prism vergences for near and far had no relation to their complaints. In fact, some who should have been uncomfortable according to their prism vergence ratio had no complaints at all. It is evident, therefore, that it is not the duction power per se, but, rather, the patient's threshold of sensitiveness, that is important for ocular comfort. If this is low and the strain is too great, the body rebels and symptoms of ocular or juxtaocular discomfort result in susceptible persons.

*Orthoptic Training.*—The purpose of orthoptic training of adults is to produce comfortable binocular vision. Healy<sup>6</sup> discussed "symptom-free" and "symptom-producing" heterophorias and emphasized that the

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5. Allan, F. N.: The Clinical Management of Weakness and Fatigue, J. A. M. A. **127**:957-960 (April 14) 1945.

6. Healy, E.: Treatment of Phorias in Adults, Am. J. Ophth. **31**:703-708 (June) 1948.

patient who manifests a "symptom-free" heterophoria, regardless of the degree, is best left untreated. For best results, the process of fusional exercises necessitates a willing and cooperative patient. His improvement is related directly to his interest in the exercises. He thus replaces an uncomfortable visual reflex by a comfortable one. Bahn<sup>7</sup> recognized patients of this type and outlined a daily routine which aims at regimenting the patient's daily routine so that he has little time to think about his symptoms. In this therapy, the role of the physician and the orthoptic technician as a target of the psychiatric process of transference plays an important part in the ultimate success of relieving symptoms of discomfort.

#### COMMENT

Many of these patients have made the "rounds" of the ophthalmologists in the community. If the patient has been wearing glasses, a reduction or an increase in the power or a change in the axis of the cylinder is usually made, with only temporary relief in trial frame tests. In 1 case, three oculists changed the axis of a  $+25$  cylinder 5 to 15 degrees, with only temporary relief of symptoms. The urge to sell glasses is so great that it often prejudices the ophthalmologist in prescribing glasses when he knows they will do little good. Derby<sup>8</sup> stated that "there is entirely too much changing of lenses a fraction of a diopter or a few degrees of axis among us [ophthalmologists] and naturally so because it is the path of least resistance." In a review of 1,000 consecutive single vision prescriptions of a moderate-sized optical house, it was found that 200 were in the group of  $-25$  or  $+25$  cylinders or less. Of these 200 prescriptions, a not too small portion consisted of  $+$  or  $-12$  spheres or cylinders. Thus, in this community at least, approximately 20 per cent of the prescribed single vision lenses are worn by patients whose benefit cannot be attributed to the optical effect of the lenses alone.

The majority of these patients will be found to have been fairly comfortable up to a certain point in their lives, when their train of symptoms emerged. At that time, if an ocular examination was conducted, a small refractive error may or may not have been found; a muscular imbalance was usually discovered with a disturbance in the accommodation-convergence relation. If the same patient were examined before his symptoms developed or after his symptoms subsided, a similar small refractive error would be found and the prism vergences would not be changed too greatly (unless an educational process has been entered on through the medium of orthoptics). The ocular findings per se will not result in symptoms of ocular or juxtaocular discomfort, but the response to a situation in life or to a series of accumulative experiences

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7. Bahn, C. A.: The Psychoneurotic Factor in Ophthalmic Practice, *Am. J. Ophth.* **26**:369-378 (April) 1943.

8. Derby, G. S.: Ocular Neurosis, *J. A. M. A.* **95**:913-917 (Sept. 27) 1930.

in life may result in symptoms of ocular discomfort in a susceptible person. If the emotional development has been normal, the symptoms will subside without much ado, but if it has been retarded symptoms will persist. The cure lies in the physician's understanding the emotional background of the patient and in the patient's readjusting his thinking and mode of living.

An illustrative case is that of a patient of the bifocal age who had seventeen pairs of glasses prescribed in three years. He was subject to frontal headaches, which prevented him from working at his desk for any length of time. He was seen by seven or eight ophthalmologists, several nose and throat men and several general practitioners. Each told him he could not find anything wrong. The otolaryngologist removed his tonsils. Each ophthalmologist changed his prescription slightly once or twice. From the patient's history, it was learned that when he took a three month vacation he had no headache and enjoyed his reading. His glasses were correct for pupillary distance in far and near vision and were of equal power. It was learned that he was insecure at his job, and it appeared that his headaches were an escape which he was able to use whenever responsibilities were too great. He was told that there was nothing wrong with his eyes, for if there were he should, by all rules, be just as uncomfortable with them on his vacation as he was at his job. He volunteered the information that when he worked in his garden he was relieved of his headaches for several days. He was encouraged to get out-of-doors for more of his activities and obtained some relief from his symptoms; but, because of the prolonged fixation of his symptoms, it was difficult for him to modify his manner of thinking and feeling. Although he did get relief from his headaches for various periods, he had used the protective shade of his headache for so long that he could not give it up entirely.

If one treats the eyes merely as optical units, correcting whatever minor defects may be found, one cannot hope to obtain a cure of the symptoms when the eyes are merely the portals through which a deranged emotional system gives vent to its inability to live within its means. It cannot be denied that the mere wearing of weak lenses will often be sufficient to give a person temporary relief from his symptoms. There is no way to determine whether the optical correction of the small refractive error was sufficient to raise the threshold of irritability and give relief or whether the psychologic effect of the weak lenses was enough to counteract (cortically) the results of a minor emotional upset. One might say: "If the lenses give relief, who cares in what manner they do this; but if they do not, then one must seek the cause elsewhere." Of course, when glasses are given the patient with a verbal psychologic vehicle that they will help, the element of suggestion, together with the factor of transference, comes into play, and the lenses merely become

the symbol of a minor psychiatric ritual. In this case, and the patient is temporarily relieved, one might say: "Why bother?" However, among these patients are persons whose emotional stability is poor; and if the physician does not recognize the personality patterns, he may allow the patients to continue into a neurotic morass, from which, at a later period, they may need a major psychiatric "over-haul" to make them useful to themselves, to their families and to their community.

#### MECHANISM

The evolution of ocular discomfort may be explained in the following manner: When the stress of living begins to affect a susceptible person, something occurs in that person which causes him to react with more than normal lability to the ordinary situations in life. This sensitivity is a manifestation of a lowered cerebral threshold to a trying situation. The normal person soon learns to adjust himself to the situation, and there is no conflict. However, in the susceptible person the conflict causes an undue amount of concern, which acts through the hypothalamus to produce symptoms. Ill sustained accommodation, transient weakness of accommodation and excessive accommodation may occur, as do other disturbances of the autonomic system, at times of worry or emotional stress.<sup>9</sup> There is reflex distention of the cerebral arteries, with radiation of pain in the region of distribution of the ophthalmic branch of the fifth nerve. A reflex spasm of the ciliary body may be produced, with resulting ciliary pain. The patient, therefore, complains of blurring of print, so that it takes him a moment to get things into focus, by blinking or by momentary forceful concentration. He complains of photophobia without any evidence of organic change within the eye. He may also complain of seeing double when he is tired.

#### TREATMENT

Treatment of such a patient should consist, first, of obtaining a good history of the onset and course of his present complaints. The patient should be permitted to tell his story in his own, unchronologic way, for from this account one can often learn whether the condition is functional or organic. A complete examination of the eyes, including refraction with cycloplegia, should be made. In his study, the physician must have an interest in and understanding of human beings and their problems, as well as knowledge and understanding of diseases in general. In many cases one may be on the receiving end of an emotional catharsis, and merely the lending of a sympathetic ear to the patient's discharge of emotional tension may be all that is needed. In other cases the relation of the emotion to the symptoms may be explained to the patient, or, better

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9. Cogan, D. G.: Accommodation and the Autonomic Nervous System, *Arch. Ophth.* **18**:739-766 (Nov.) 1937.



still, the patient may be permitted to realize this himself, so that at the postcycloplegic examination this realization will be complete. In the more resistant cases the patient's confidence is not won, and it may be necessary to have the element of time enter into the picture, so that the factor of transference may take place. The use of placebos, such as vitamin preparations and small doses of phenobarbital, may permit one to gain this element of time. Of course, the danger in the use of placebos may be a fixation in the patient's mind that something is actually wrong—otherwise the physician would not give him medicine. The real danger in treatment in these cases is to overlook a truly ocular cause that is amenable to ophthalmologic therapy and to call such a case one of ocular neurosis. On the other hand, it is just as much an error to continue to treat the patient from the standpoint of the eyes when the service of a trained psychiatrist is indicated.

Davis<sup>10</sup> stated the belief that the ophthalmologist should treat these patients rather than refer them elsewhere (unless for diagnostic work-up), for, in his opinion, the ophthalmologist is in an ideal position to care for the patient because of the nature of the complaints. As long as ophthalmology consists in caring for patients from a medical, as well as from an ophthalmologic standpoint, many of these patients can be turned early in their neurotic course.

It appears, therefore, that what really must be treated in these patients is their emotional sensitivity and the ideas which are behind their sensitivity. The patient should be told, after a thorough examination, that his eyes are normal. It then becomes a matter of having him understand the manner of his thinking and feeling toward conditions and people with whom he is associated. In other words, a reeducational program is started, and the patient is taught to develop a new mode of thinking and of reacting to various life situations. When the patient learns to adapt himself to his problem, there is no conflict and, as a result, no symptoms.

#### CONCLUSIONS

Persons with ocular discomfort of nonorganic nature have personality characteristics of a definite pattern. Relief of their symptoms consists in helping them to understand their emotional background and directing their energies into less conflicting channels.

1221 Victoria Street (34).

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10. Davis, W. T.: *Astenopia and Headaches Not of Ocular Origin*, New Orleans M. & S. J. **88**:159-167 (Sept.) 1935.

# Case Reports

## TERATOMA OF ORBIT

CAPTAIN F. HARBERT (MC), U.S.N.

**C**ONGENITAL tumors are classified embryologically according to the number of germ layers from which the tumor is derived. Thus, osteoma and angioma are derived from a single germ layer. Dermoids are characterized by tissue derived from two germ layers, viz., ectoderm and mesoderm. These tumors are characterized by the presence of squamous epithelium and of its derivatives, such as hair, nails, teeth and sudoriferous and sebaceous glands. The dermis, derived from underlying mesenchyme, may become differentiated to form cartilage, bone, fat, muscle or other specialized tissue. Dermoids may occur as cysts or solid tumors. In the cyst, the dermis is on the outside and the epithelium lines a cavity, usually filled with inspissated, oily secretion and hair. In the commoner, solid type, the epithelium is exposed to the surface of the body, and a common site is astride the corneal margin. Solid dermoids are commoner than the cystic variety about the orbit.<sup>1</sup>

The commonest locations of dermoid and teratoma are the ovaries, testes and sacral regions, but they have been reported in nearly every part of the body. An analysis of dermoid cysts seen at the Mayo Clinic from 1910 to 1935 showed that of 1,495, 45 per cent occurred in the postanal region, 42 per cent in the genitalia, 7 per cent in the head and neck and 6 per cent elsewhere.<sup>2</sup> Of the dermoids of the head and neck, one half were in the orbital region, and of these 60 per cent occurred in the outer third of the eyebrow. Half of these were noted at birth. Only 10 per cent of the dermoids of the orbital region (6 in twenty-five years) were within the orbit, usually in the upper outer quadrant of the right orbit.

True teratomas must contain tissue derived from all three germ layers. Such tumors are exceedingly rare in the orbit and are usually

From the United States Naval Hospital, Philadelphia.

Read at a meeting of the College of Physicians of Philadelphia, Section on Ophthalmology, Dec. 18, 1947.

This article has been released for publication by the Division of Publications of the Bureau of Medicine and Surgery of the United States Navy. The opinions and views set forth are those of the author and are not to be construed as reflecting the policies of the Navy Department.

1. Rosen, E.: Bilateral Teratoid Tumor of the Limbus, *Arch. Ophth.* **32**: 120-122 (Aug.) 1944. Sherman, A. R.: Teratoid Tumor of the Conjunctiva and Other Development Anomalies with Naevus Verrucosa of the Scalp, *ibid.* **29**: 441-446 (March) 1943. Badier, G.: Solid Dermoid of the Lid Border, *Bull. Ophth. Soc. Egypt* **34**:65-67, 1941.

2. New, G. B., and Erich, J. B.: Dermoid Cyst of Head and Neck, *Surg., Gynec. & Obst.* **65**:48-55, 1937.



Fig. 1.—Appearance of child on day after birth (Dec. 11, 1946).



malignant.<sup>3</sup> Identification of tissue derived from the endoderm is sometimes difficult, and some pathologists rely on the complexity and variety of tissue in making a diagnosis of teratoma. The finding of tissue con-

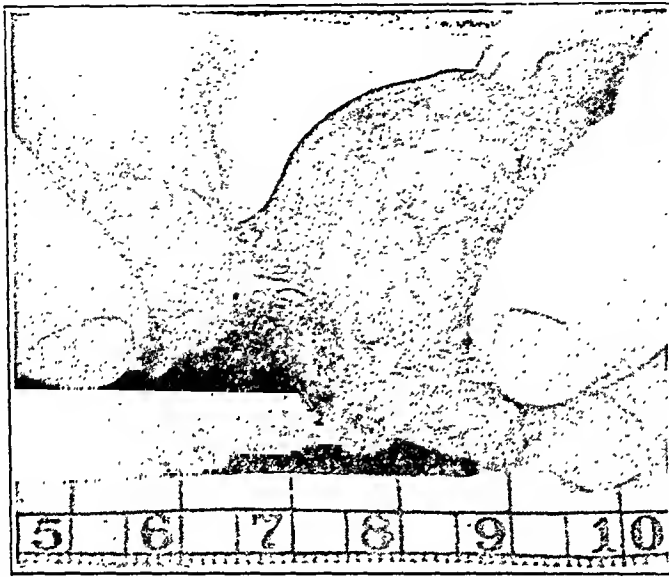


Fig. 3.—Excised specimen, showing optic nerve entering tumor.

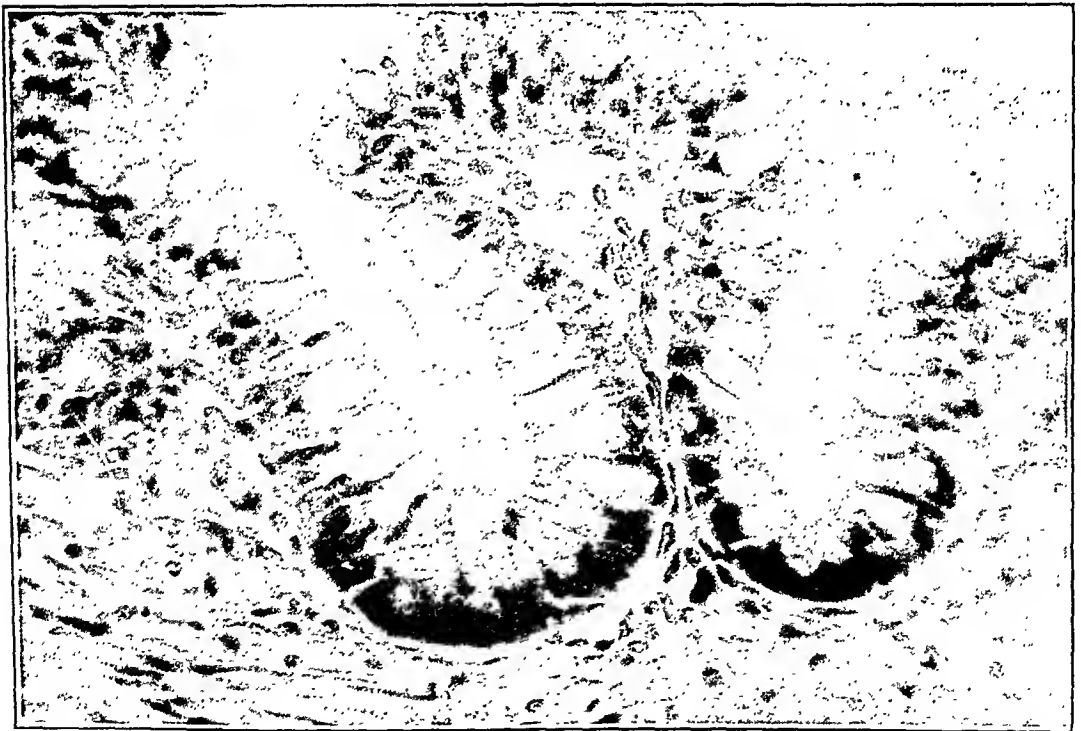


Fig. 4.—Mucous membrane with goblet cells in characteristic arrangement of the intestine.

3. (a) Samuels, B.: Dermoid Cysts of Orbit, *Tr. Am. Ophth. Soc.* **34**: 226-230, 1936. (b) Mann, I.; *Developmental Anomalies of the Eyes*, London, Cambridge University Press, 1937, pp. 411-412. (c) Burnier, P., and Salles, M.: Teratoma of Orbit, *Arq. Inst. Penido Burnier* **7**:114-128, 1945.

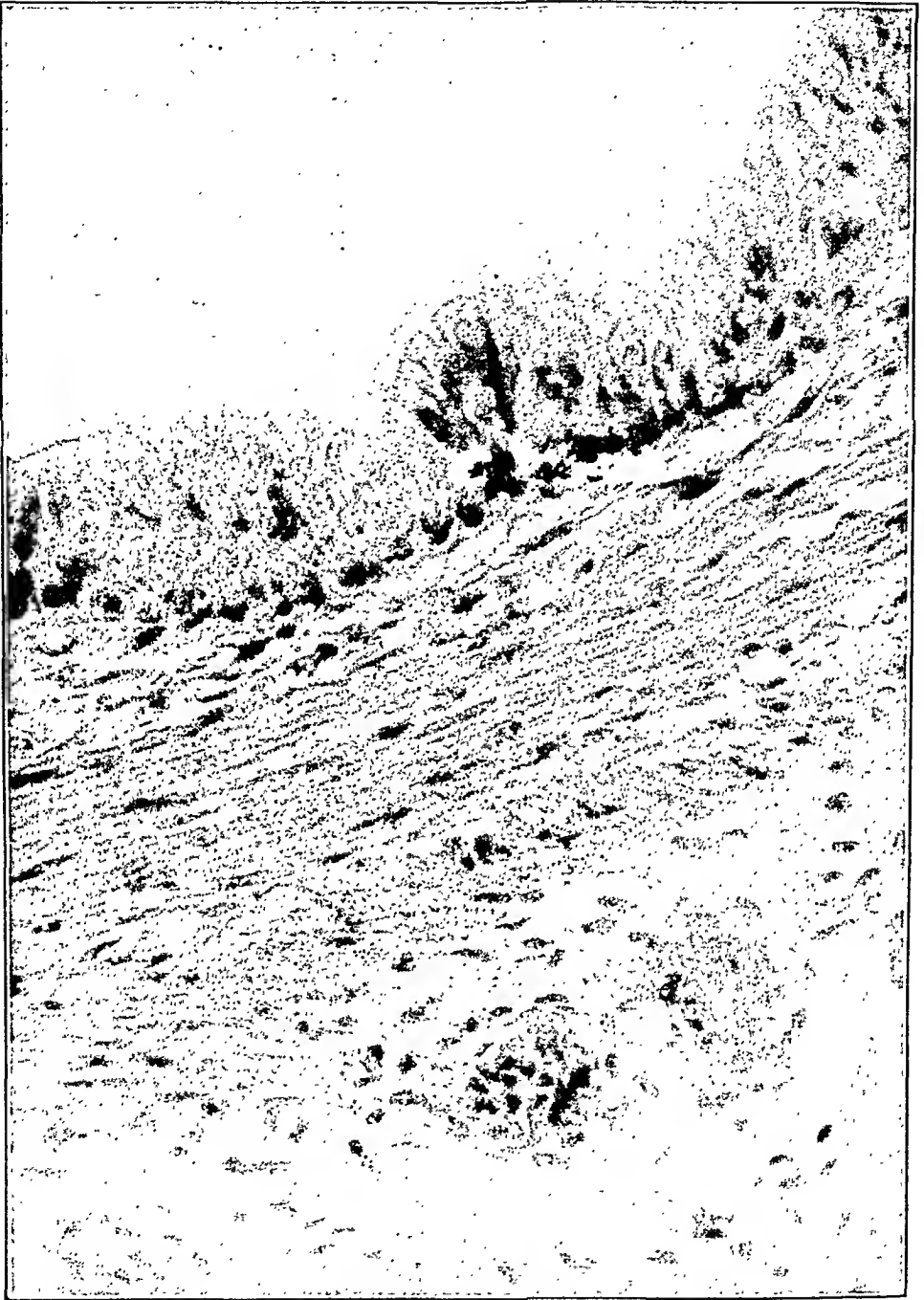


Fig. 5.—Ciliated columnar epithelium.

sisting of cavities lined with pure mucous epithelium with an arrangement characteristic of gut is considered diagnostic of endodermal origin. The dermoid variety is often referred to in the literature as teratoma, teratoid tumor, mixed tumor or epibulbar tumor.

A perusal of the literature for the past ten years revealed only 1 case of teratoma of the orbit.<sup>3c</sup> This case was very similar to the case reported here in that the tumor was present at birth, an intact eye surmounting the tumor. This eye was permitted to ulcerate, operation being deferred for two months. A cleavage line was easily found, and exenteration of the orbit resulted in an apparent cure at the time of reporting, two years later. The clinical diagnosis was confirmed



Fig. 6.—Young bone with central marrow cavity and bone marrow.

pathologically. A review of the literature by Burnier and Salles indicated that 17 cases of true orbital teratoma had previously been reported.

#### REPORT OF A CASE

Baby M. was born Dec. 11, 1946 with a very large mass in the left orbit, causing pronounced proptosis. At birth the conjunctiva and cornea were normal, but within twenty-four hours the conjunctiva became increasingly chemotic and the cornea showed beginning cloudiness and infiltration. This process continued in spite of moist chamber dressings during the following two days, before permission for operation was obtained. The cornea was well formed and measured 9 mm. in diameter. The globe could be palpated through the mass and seemed to be

flattened anteroposteriorly. Behind the globe a solid tumor filling the entire orbit could be palpated. The outline of the mass was smooth except inferiorly, where several nodules were felt. Transillumination of the mass revealed the same consistency as that of the cheek. The globe was transilluminated clearly. A



Fig. 7.—Atypical structure lined with ciliated columnar epithelium.

needle passed into the mass for diagnostic aspiration failed to reveal fluid. The eye was not fixed, but motion was restricted to random, irregular, very slow oscillations.

The iris of the right eye was normally blue, but that of the proptosed eye was dark brown. The pupil was miotic but dilated well with atropine. Examination with the slit lamp showed persistence of a well marked marginal vessel in

the pupil. Roentgenograms of the orbits showed distinct enlargement of the left orbit, with intact bony walls.

Physical examination revealed no other developmental defects, and the right eye was normal. A clinical diagnosis of microphthalmos with cysts was made, and exenteration of the orbit was advised at once to prevent deep infection of the

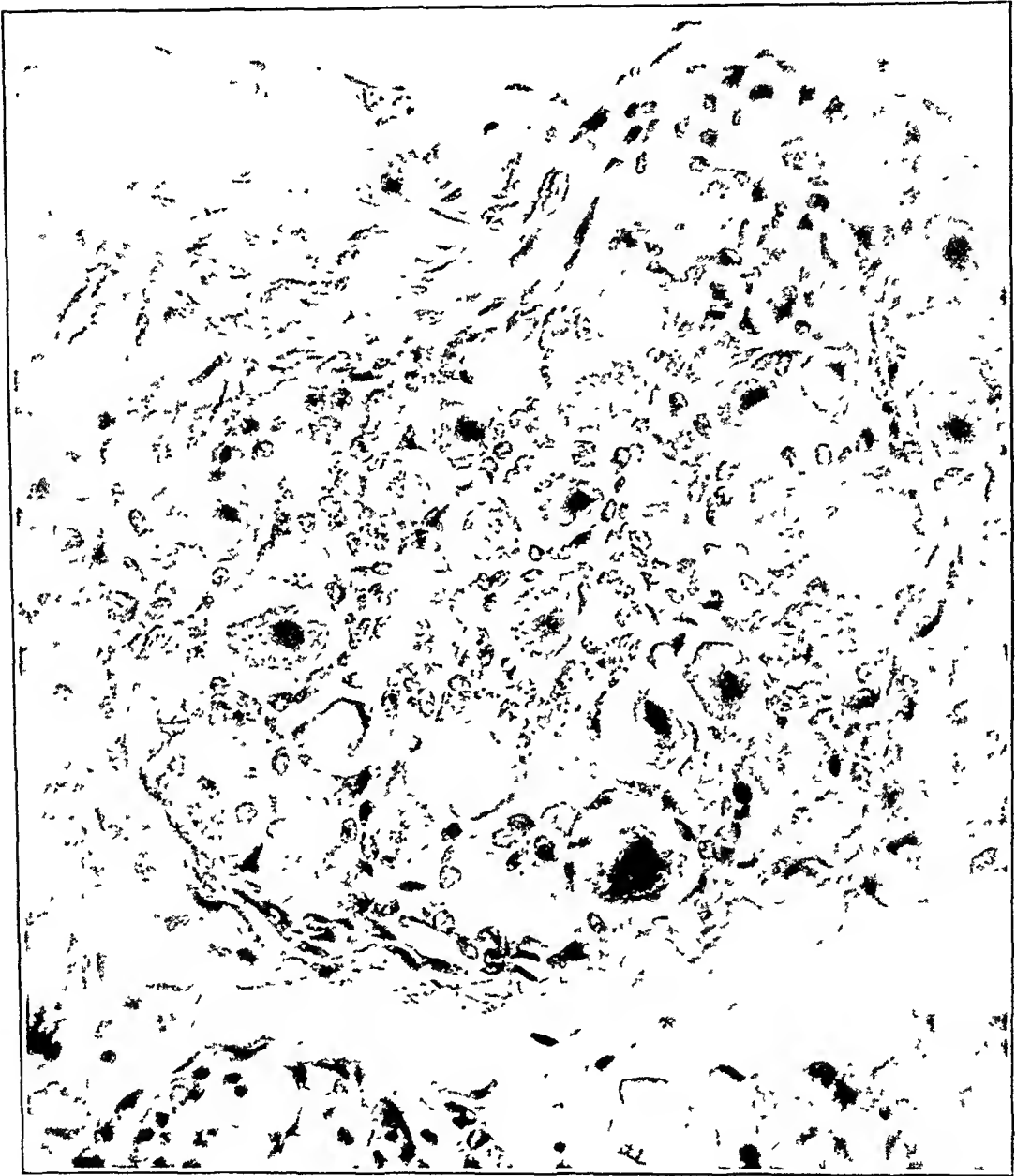


Fig. 8.—Large ganglion cells.

eye and orbit, which was considered inevitable because of exposure and edema.<sup>4</sup> Permission for operation was obtained on the third day.

Operation was performed with infiltration anesthesia, with no objection from the patient except to the injections. Two per cent procaine hydrochloride with epinephrine hydrochloride (1:1,000) was injected into the lids and along the

4. Duke-Elder, W. S.: *Text-Book of Ophthalmology*, St. Louis, C. V. Mosby Company, 1941, pp. 1268-1274.



orbital walls to the apex in minimal amounts and the conjunctiva was anesthetized by instillations of tetracaine hydrochloride U. S. P. The conjunctiva was first separated at the limbus on the temporal side, and the globe and outer aspect of the mass were exposed to ascertain the relation of the mass to the eyeball and to determine whether the mass was resectable without sacrificing the eye. It soon became apparent that the optic nerve passed through, and seemed an integral part of, the mass and that the extraocular muscles and Tenon's capsule were so attenuated that they were not recognizable. An incision into the exposed mass showed that it was composed of solid tissue with multiple cysts containing clear fluid. A line of cleavage between the mass and the periorbita was readily obtained, and the mass was easily separated.

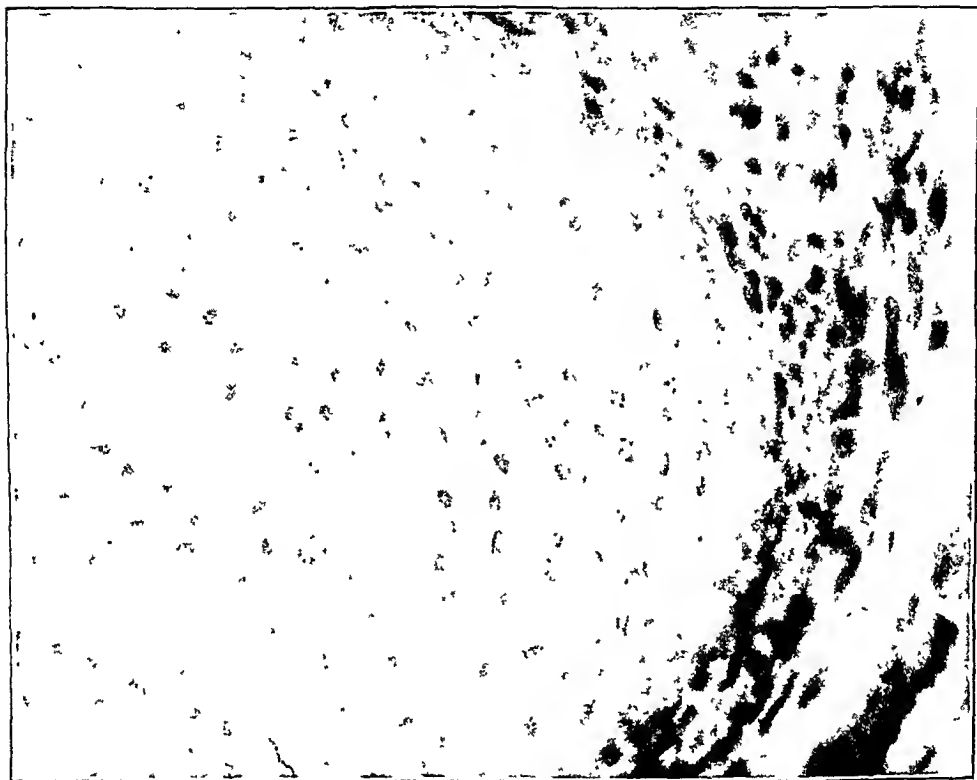


Fig. 9.—Young cartilage.

The entire orbit was filled with tumor, the mass extending to the orbital fissures and the optic foramen. When the eye and the mass were removed, a plastic implant was placed in the apex of the orbit and the conjunctiva was closed over it. A conformer was inserted in the conjunctival sac. When healing was completed and contraction of the cul-de-sac had been established, the conformer was replaced with an acrylic prosthesis made from a casting of the cavity. This has been worn continuously since (fig. 2).

Measurement of the excised specimen showed the globe to be 18 by 19 mm. at the equator and 15 mm. in the anteroposterior axis. The retrobulbar mass was roughly 5 by 4 cm. and contained multiple cysts on the surface (fig. 3).

Convalescence was uneventful, and the child is developing normally, with no evidence of recurrence to date.



Fig. 10.—Squamous epithelium with hair follicles and sebaceous glands.

*Pathologic Study.*—Microscopic sections of the excised specimen were examined by Dr. J. S. Friedenwald at the Wilmer Institute. His diagnosis was teratoma of the orbit, microphthalmos, exposure keratitis and hypopyon ulcer of the cornea.

The globe was rather small. The cornea was infiltrated and scarred. The anterior chamber was filled with polymorphonuclear leukocytes. Many such cells were seen in the iris stroma, and there was an abscess in the ciliary body. There were many retinal and subretinal hemorrhages and a few tiny choroidal hemorrhages. The optic nerve showed partial atrophy.

The tumor was a large cystic mass containing fat, bone, cartilage and many cysts, which were lined with epithelium of varying forms. The epithelial forms included squamous epithelium with many hair follicles and sebaceous and sudoriferous glands, ciliated columnar and cuboidal epithelium and mucous membrane with a papillary structure and arrangement characteristic of intestine. There were also small scattered glands of the racemose type, resembling salivary or lacrimal glands.

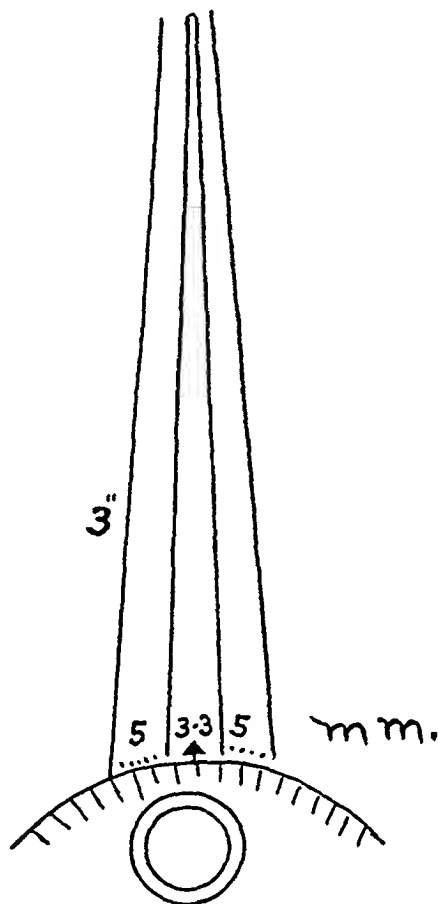
The matrix of the tumor was young connective tissue. Embedded in this matrix were lymphoid follicles with germinal centers, bone marrow and nerve tissue, including large ganglion cells.

# Clinical Notes

## SUSPENSION OF UPPER LID DURING INTRAOCULAR OPERATIONS

PAUL C. CRAIG, M.D.  
READING, PA.

IT HAS been found convenient and satisfactory to dispense with speculum and retractors for intraocular operations, particularly during the critical stages. In their stead an upper lid suture is used, which is described here.



Placement of suture in the upper lid.

### UPPER LID SUTURE

*Suture Material.*—The suture is twisted 0000 black silk with atraumatic needle, 18 inches (45.7 cm.) long.

*Placing of Suture.*—The needle is introduced through the thickness of the skin of the upper lid 8 mm. to one side of the center of the lid margin, immediately above and as close to the cilia as possible. It is passed toward the midline and emerges 5 mm. from the point of entrance immediately above and as close to the cilia as possible. It is pulled through, leaving an end about 3 inches (7.5 cm.) long. It is now reintro-

From the Department of Ophthalmology, St. Joseph's Hospital.

duced 6 mm. from the point of exit, again immediately above and as close to the cilia as possible. It emerges 5 mm. from the point of entrance. A loop is formed between the two stitches, and this loop is made as long as the tail end of the suture. The needle end of the suture is cut to correspond to the length of the loop and the tail end.

*Use of Suture.*—Throughout the operation an assistant holds the loop and both ends of the suture between thumb and forefinger, giving a four point suspension of the lid. The assistant has an opportunity to lift, or rather to "carry," the lid, or he can relax it completely, as the progress of surgical procedure may indicate.

#### COMMENT

The department of ophthalmology of St. Joseph's Hospital at present uses thorough block akinesia and anesthesia, as well as the Atkinson retrobulbar injection for the lowering of intraocular pressure.

The next step in any intraocular procedure is the placement of the lid suture. A speculum is used for dissection of the conjunctival flap and for the corneoscleral suture, only if desired. At the end of the operation the lid suture is removed provided the lid margins can be approximated. If, however, the lid fissure remains open, the loop of the lid suture is pulled out and the two ends are fastened to the skin of the cheek with Scotch tape. The ends of the suture are now about 6 inches (30 cm.) long and are doubly reversed over the Scotch tape for better anchorage.

It may be of economic interest to know that the cut end of the lid suture with needle is utilized as a hammock suture for the superior rectus muscle. It is approximately 6 inches long and lends itself well to this purpose.

Experience has shown that "carrying" the upper lid appears to reduce the incidence of gaping of the incision. If vitreous should present itself, it seems to withdraw more readily on appropriate manipulation of the upper lid.

#### SUMMARY

An upper lid suture is described which may make intraocular procedures somewhat safer.

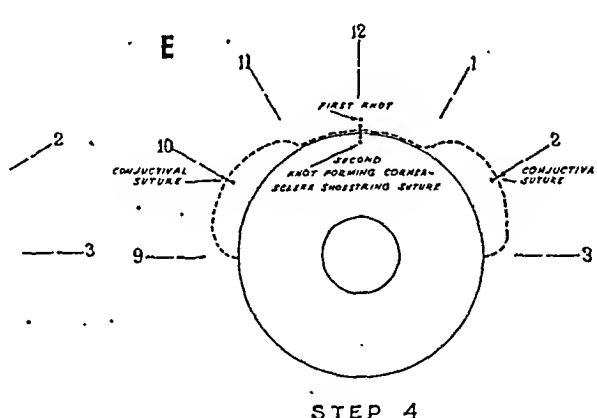
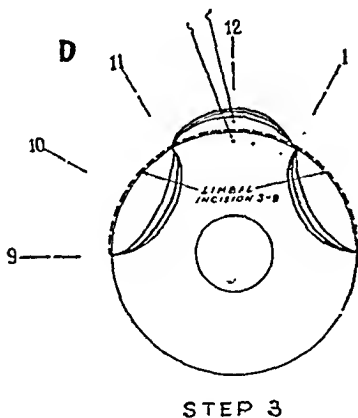
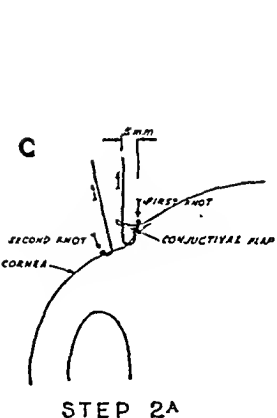
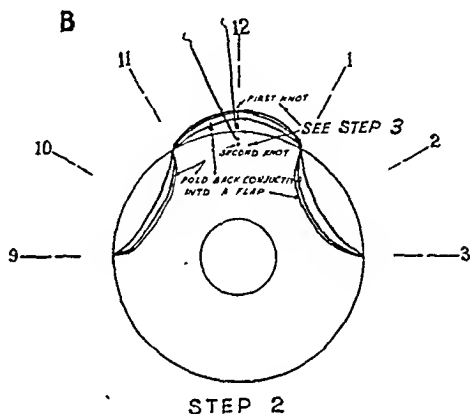
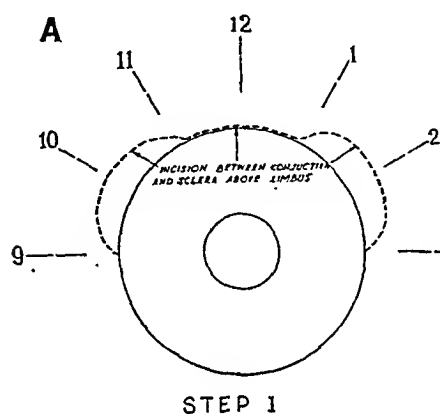
St. Joseph's Hospital.

## A NEW SHOESTRING CORNEOSCLERAL SUTURE

GERALD D. SPERO, M.D.  
DETROIT

I should like to recommend the following corneoscleral suture with modified conjunctival flaps.

1. A conjunctival incision is made along the limbus from 11 to 1 o'clock (figure, *A*). This part of the conjunctiva is then undermined



Steps in placement of a new shoestring corneoscleral suture: *A*, step 1; *B*, step 2; *C*, step 3; *D*, step 4; *E*, step 5.

From 1 to 3 o'clock a conjunctival flap 3 mm. wide is prepared. A similar one is made from 11 to 9 o'clock (figure, *B*).

2. A single-armed 000000 silk suture is knotted double. The needle is then introduced into the conjunctiva above 12 o'clock, about 5 mm. from the limbus, from without in. A vertical bite is then taken in the episclera 2 mm. above the limbus, the needle emerging as close as possible to the limbus. The needle is then reintroduced through the conjunctiva 2 mm. above the free border and brought out. This needle is then cut off. The suture is now anchored above in the episclera and outside the conjunctiva.

3. A second needle, similarly knotted, is introduced vertically in the cornea 2 mm. below the limbus at 12 o'clock and brought out as close to the limbus as possible. The needle is cut off and the thread pulled taut. There are now two threads, one below, anchored by a knot in the cornea, and the other above, in the episclera (figure, *C*).

4. After the sutures are ready, an incision is made, preferably with a keratome, along the limbus and enlarged with scissors (figure *D*).

5. When the lens is extracted, the central sutures are tied with a double loop. This prevents slipping of the suture. Two corneoscleral sutures, instead of one, can be used. After the iris is replaced, the conjunctival sutures are put in and tied (figure, *E*).

This suture has the following advantages:

1. The shoestring suture is easy to introduce.
2. The double knot does not cause any irritation to the cornea.
3. Introduction of sutures before section is much simpler than after.
4. There is practically no danger of cutting the sutures, for they are already cut. There are no loops in the way.
5. The closure is more rapid, and therefore complications, when they occur, can be handled with greater ease.
6. The lower suture is anchored into the corneal flap. By pulling on it slightly, the surgeon can get an excellent view of the lens during its extraction.
7. The absence of the conjunctival flap in the center permits greater visibility when the cataract incision is made. Enough conjunctiva remains, and conjunctival sutures can easily be introduced on either side of 12 o'clock.

Miss Connie Davis and Mr. Arnold assisted in preparation of the sketches for this article.

2311 David Broderick Tower (26).

# Ophthalmologic Reviews

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## NEUROMYELITIS OPTICA (DEVIC'S DISEASE)

Presentation of Five Cases, with Pathologic Study, and Review of Literature

FREDERICK C. STANSBURY, M.D.

SYRACUSE, N. Y.

*(Concluded from Page 335)*

### PATHOLOGIC FEATURES

The optic nerves received special attention from the early investigators of neuromyelitis optica. These writers stated that the pathologic condition of the spinal cord was an ordinary acute myelitis and that the involvement of the optic nerves represented an extraordinary pathologic phenomenon. The loss of myelin sheaths in the optic nerves was first recorded by Achard and Guinon,<sup>6</sup> who described almost complete disappearance of myelin in the optic nerves of their patient. Elschnig<sup>11j</sup> verified their observations in his case and described intraocular lesions; he noted extreme thinning of the nerve fiber layer of the retina, with diminution of the ganglion cells. Dalen<sup>11q</sup> reported the same alterations in the retinas of another patient with this disease. Dreschfeld<sup>11i</sup> wrote an excellent pathologic report of a case, in which he described perivascular infiltration and irregularly distributed patches of demyelination throughout the lesions. The centers of the optic nerves in Dreschfeld's case were completely destroyed; he observed sclerosis of the periphery of the nerves, with conversion of this portion into a mass of connective tissue. In 2 cases in which autopsy was performed Holden<sup>60</sup> noted areas of softening in the spinal cord, with rarefaction of tissue, glial overgrowth in places and extensive cellular infiltration about the blood vessels.

In the case published by Devic,<sup>7</sup> the lesions were observed in the periphery of the optic nerves; the myelin sheaths in these foci had not completely disappeared, although the remaining myelin was fragmented and discontinuous for considerable distances. Devic described perivascular spaces crowded with small round cells and infiltration of the interstitial tissue of the nerves with these same cells. He also reported the destruction of myelin sheaths and disintegration of anterior horn cells in the spinal cord. Katz<sup>11n</sup> found that the optic nerves were grossly much reduced in size and that microscopically the centers of the nerves were completely degenerated. In a monograph containing detailed, minute observations on the pathologic changes in 4 cases, Bielschowsky<sup>62</sup> described destruction of the optic nerves as far back



as the chiasm in 1 case and degeneration through the whole optic pathway in another. There were scattered areas of softening, with infiltration of round cells about the blood cells running into these foci. In the severe lesions Bielschowsky noted destruction of nerve fibers, increased interstitial connective tissue, proliferation of neuroglia and collections of fatty granular cells.

In his review of neuromyelitis optica, Goulden<sup>10</sup> discussed the autopsy findings in 14 cases. He described early demyelination of the optic nerves in a necrotic process that eventually caused complete destruction of the nerve fibers. Goulden found infiltration with round cells very common but neuroglial proliferation to form scar tissue uncommon. Abelsdorf<sup>18c</sup> discussed the findings in an interesting case in which the process extended through both optic nerves, the chiasm and the left optic tract; he expressed the belief that Devic's disease was a parenchymatous inflammation of the nerve tissue proper. In the pathologic discussion of his case, Beck<sup>12</sup> described massive demyelination of the cord and optic nerves and four types of cellular reaction: (1) round cell perivascular infiltration, (2) multiplication of blood vessels, (3) neuroglial proliferation and (4) polymorphonuclear cell infiltration of the tissues. In sections prepared by Bielschowsky's silver impregnation technic, Beck observed small areas of rarefaction in which even the axis-cylinders were destroyed; he expressed the belief that these lesions distinguished this disease from disseminated sclerosis. Michaux<sup>30</sup> described the three most likely sites for the initial lesion: (1) the upper dorsal segments of the cord, (2) the hypothalamic region and (3) the optic chiasm. Microscopically, Michaux observed the process to be essentially one of necrosis, the distinguishing features of which are (1) the irregularity of the lesions, (2) the intensity of the demyelination and (3) the destruction of axis-cylinders.

Balser,<sup>18</sup> reporting on the pathologic study of 3 cases of neuromyelitis optica, suggested that the lesions are initially perivascular and focal, and that they later extend or coalesce, so that there appears to be a central core of destruction. He stated that this process in the spinal cord tends to be continuous rather than spotty, often involving a number of consecutive segments in a linear lesion. Histologically, according to Balser, there are proliferation of blood vessels and infiltration of the tissues with lymphocytes, plasma cells and a few polymorphonuclear leukocytes; the axis-cylinders show thickening, fragmentation and end bulb formation. There is slight or no proliferation of neuroglial fibers in the early, nonremissive stage, Balser found; but a dense, fibrous connective tissue overgrowth may occur later in the disease. Cone, Russel and Harwood<sup>15</sup> reported intense glial scarring in their case, with the formation of dense plaques in the cerebrum and cerebellum. Markiewicz and Peters<sup>45</sup> commented particularly on the

TABLE 2.—Pathologic Changes in 20 Cases with Autopsy

Case No.	Author	Distribution of Lesions Optic nerves, chiasm, optic tracts and spinal cord	Demyelination	Loss of Axis-Cylinders	Neuroglial Proliferation	Perivascular Infiltration	Proliferation of Oculiferous Glands	Cavitation
1	Beck .....	Optic nerves, chiasm, optic tracts and spinal cord	"Massive"	+	Astrocytosis; some microglia; many gitter cells	Lymphocytes, polymorphonuclear cells, plasma cells, and gitter cells	Great multiplication	Optic nerves, tracts, chiasm, and spinal cord
2	Walsh .....	Cerebral cortex, basal ganglions, optic nerves, chiasm and spinal cord	"Intense"	+	"Slight"	"Minimum"	..	Spinal cord
3	Frank and DeJong .....	Lumbar section of cord (only part examined)	"Complete"	"Complete"	"Countless microglia"	"None"	..	..
4	Balscr (case 1) .....	Optic nerves, chiasm, geniculate bodies, hypothalamus and spinal cord	"Entire optic tract"	+	"Very little"	Lymphocytes, polymorphonuclear cells, and plasma cells	+	..
5	Balscr (case 2) .....	Brain, optic tracts and spinal cord (optic nerves not obtained)	Present	+	None in the cerebrium, very little in the spinal cord	Lymphocytes, occasional polymorphonuclear cells and plasma cells	"Quite marked"	Spinal cord
6	Balscr (case 3) .....	Spinal cord (only part examined)	"Diffuse"	+	"Very little"	Lymphocytes, polymorphonuclear cells, and plasma cells	+	..
7	Dolgopol .....	Spinal cord, medulla and optic nerves	"Extensive"	—	Some astrocytosis; little microglial reaction	Lymphocytes and plasma cells	..	..
8	Cone, Russel and Harwood .....	Brain, cerebellum, optic nerves, chiasm and spinal cord	Present	+	.....	Rare lymphocytes	..	Spinal cord
9	Noran and Polan .....	Optic nerves, spinal cord and lower part of medulla	"Extensive"	+	Astrocytes and microglia	Lymphocytes	+	Spinal cord
10	Kohut and Kleiter .....	Right optic nerve, lower part of medulla and spinal cord	"Severe, patchy," Present	+	Hyperplastic astrocytes and increased microglia	Lymphocytes, with some histiocytes	..	Spinal cord
11	Husslin .....	Right optic tract, right cuneus, internal capsule and spinal cord	Present	+	Some astrocytosis; great increase in microglia	Lymphocytes and gitter cells	"Many new capillaries"	..
12	Hurst, de Orespigny and Fry .....	Optic nerves, chiasm, optic tracts, geniculate bodies and spinal cord	"Extensive"	+	Great increase in microglia	Widespread lymphocytes	..	..
13	McAlpine (case 1) .....	Optic nerves and spinal cord	"Diffuse"	+	Moderate macroglial reaction; marked microglial reaction	None	"Slight increase"	..
14	McAlpine (case 2) .....	Optic nerves, chiasm, left optic tract, lower part of medulla and spinal cord	"Diffuse"	+	Moderate macroglial reaction; marked microglial reaction	Slight, lymphocytes	+	Spinal cord
15	Lowenberg, DeJong and Foster .....	Optic nerves, some of the spinal nerves and spinal cord	.....	+	Increase in the macroglia and microglia	Lymphocytes	+	+
16	Stansbury (case 1) .....	Optic nerves, lower part of medulla and spinal cord	Present	+	Moderate astrocytosis and a great increase in microglia	Lymphocytes, plasma cells and occasional monocyte	..	..
17	Stansbury (case 2) .....	Cerebral cortex (one small lesion), right optic nerve and spinal cord	"Massive"	+	Moderate astrocytosis and a great increase in microglia	Lymphocytes and plasma cells	..	..
18	Stansbury (case 3) .....	Right optic nerve, lower part of medulla and spinal cord	Present	+	Moderate astrocytosis and a great increase in microglia	Lymphocytes and plasma cells	..	Spinal cord
19	Stansbury (case 4) .....	Optic nerves and pons	"Extensive"	+	Moderate astrocytosis and a great increase in microglia	Lymphocytes, plasma cells and occasional monocyte	..	..
20	Stansbury (case 5) .....	Cerebral cortex, basal ganglions, brain stem, right optic nerve and spinal cord	Present	+	Moderate astrocytosis and a great increase in microglia	Lymphocytes, plasma cells and occasional monocyte	..	..

absence of gliosis in their case, while Putnam and Forster<sup>27</sup> stated that chronic glial fibrosis occurs frequently in neuromyelitis optica, in addition to the acute degenerative changes.

In a study of the pathologic changes in 12 cases of neuromyelitis optica, McAlpine<sup>25</sup> found diffuse myelitis in 9 cases and disseminated focal lesions in the remaining 3 cases. The hallmark of neuromyelitis optica, according to McAlpine, is necrosis, which in the cases with diffuse myelitis is sometimes accompanied with cavitation. He stated that the response of the macroglia depends on the intensity of the lesion; when necrosis occurs not even the astrocytes are spared, and then gliosis is impossible, except at the margins of the involved areas. On the other hand, McAlpine observed that the microglia uniformly show a pronounced reaction in the form of fat granule corpuscles; the microglial elements are able to perform this function because of their motility and rapid proliferation. In his experience, proliferation of capillaries is relatively uncommon, two incompatible conditions being necessary: (1) a duration of several months and (2) severe necrosis. When the capillary reaction does occur, McAlpine explained, it is because the destruction of astrocytes and consequent poor glial reaction leave only one tissue able to effect any repair, namely, the blood vessels.

*Cerebral Lesions.*—The lesions of neuromyelitis optica are not confined to the spinal cord and optic nerves in all cases; in fact, Devic was first to mention the occurrence of cerebral foci. Jumentié and Valière-Vialeix<sup>13g</sup> described a case in which the pathologic process was centered in the brain; postmortem examination revealed a large area of softening in the left occipital lobe and numerous smaller foci in the right occipital lobe, with the characteristic changes in the optic nerves and cord. Bouchut and Dechaume<sup>13j</sup> reported a case with lesions in the spinal cord, medulla, midbrain, cerebellum and brain, in addition to those in the optic nerves. Guillain and associates<sup>31p</sup> also reported a case with pathologic cerebral changes; associated with lesions typical of neuromyelitis optica in the spinal cord and optic nerves, they noted a large necrotic area in the hypothalamic region. Demyelinated lesions in the cerebral cortex and brain stem were also described by Cestán, Riser and Planques<sup>36</sup> and by Alajouanine and associates.<sup>38</sup> Walsh,<sup>17</sup> too, found small lesions throughout the white matter of the brain and spinal cord; in his case practically all the white matter around the calcarine fissure was involved.

*Review of the Pathologic Changes in 20 Cases.*—In an attempt to better correlate the distribution of the lesions in neuromyelitis optica and to ascertain the distinctive features of these lesions, the pathologic features of the 15 cases previously discussed clinically were studied and the data combined with corresponding information for the 5 cases presented in this report. The data are presented in table 2.

Study of the pathologic picture in 20 cases reveals the following facts:

1. Distribution of the lesions was as follows:

	No. of Cases
Optic nerves (not obtained in 4 cases).....	16
Optic chiasm .....	5
Optic tracts .....	5
Cerebral hemispheres .....	5
Brain stem .....	12
Spinal cord .....	19
Cerebellum .....	1

2. Demyelination was prominent in 19 cases. It was not specifically mentioned in the remaining case, apparently by an omission.

3. Destruction of axis-cylinders was described in 19 cases.

4. Astrocytosis, usually mild, was described in 13 cases. Proliferation of the microglia, usually pronounced, was noted in 15 cases. Neuroglial proliferation, without mention of cell type, was noted as "slight" in 1 case and as "very little" in 3 cases and was not mentioned in 1 case.

5. Perivascular infiltration of lymphocytes, polymorphonuclear leukocytes and plasma cells was noted in 4 cases; of lymphocytes and plasma cells in 5 cases; of lymphocytes and polymorphonuclear leukocytes in 1 case and of lymphocytes alone in 7 cases. No infiltration was noted in 2 cases and a "minimum" infiltration in another.

6. Proliferation of capillaries was described in 9 cases.

7. Cavitation (usually in the spinal cord) was present in 9 cases.

From this review of the autopsy observations in 20 cases, we may conclude, then, that neuromyelitis optica is characterized histologically by (1) demyelination of nerves, (2) destruction of axis-cylinders, (3) mild astrocytosis and pronounced proliferation of microglia, (4) perivascular infiltration of lymphocytes, plasma cells and sometimes polymorphonuclear leukocytes, (5) proliferation of capillaries and (6) cavitation. The lesions are commonly found in the optic pathway, spinal cord and brain stem, occasionally in the cerebral hemispheres and rarely in the cerebellum.

*Composite View of Microscopic Pathology.*—The pathologic process of neuromyelitis optica passes through a number of stages, during which the reaction of the nerve tissue changes from stage to stage. Thus, the microscopic picture will vary according to the stage of the lesion being studied. Some stages appear commoner because they last longer than others, so that an observer, without careful study of many lesions, may see only one or more stages of the pathologic process.

An erroneous opinion of the nature of the disease may thus be conceived. A misunderstanding of this sort concerning the pathology of multiple sclerosis existed for many years; pathologists, seeing mainly glial scars or plaques, were misled into thinking of multiple sclerosis as a primary overgrowth of the neuroglia. In the case of neuromyelitis optica, the microscopic picture is determined by three variables: (1) the severity of the reaction in the particular lesion, (2) the age of the lesion and (3) the portion of the lesion under study. All degrees

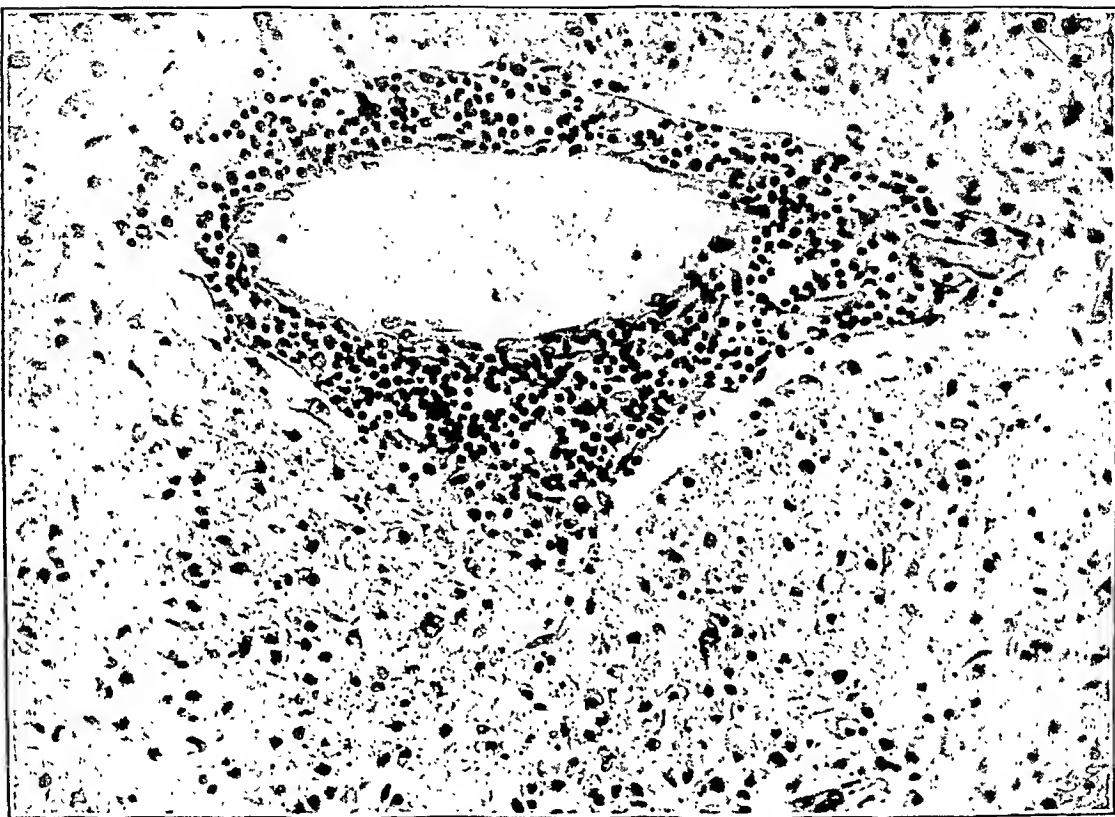


Fig. 11 (case 3).—Photomicrograph showing the typical perivascular collection of lymphocytes and plasma cells.

of severity are observed in different lesions, even in fatal cases. The age of the lesion is significant, because this process appears to run through a certain calendar of tissue reactions. Finally, the pathologic process varies within a single lesion, in that its intensity decreases from within outward. By the time the disease has caused the patient's death, most lesions are old and severe, and at autopsy many more such lesions will be found than lesions of the initial, early stage. Therefore, in order to give a better perspective of the whole process, a composite description of the microscopic events has been assembled, with photomicrographs from the 5 cases previously presented.

**Acute Inflammatory Stage:** The earliest lesion of neuromyelitis optica is an acute inflammatory process about a small blood vessel. As in inflammation elsewhere, there is exudation from the blood of fluid and leukocytes. The fluid causes edema of the sheaths of the vessel and of the tissue spaces of the surrounding parenchyma, making possible the infiltration of white blood cells. This infiltration is obviously a hematogenous one and is composed of polymorphonuclear leukocytes, lymphocytes and plasma cells. The polymorphonuclear cells are seen

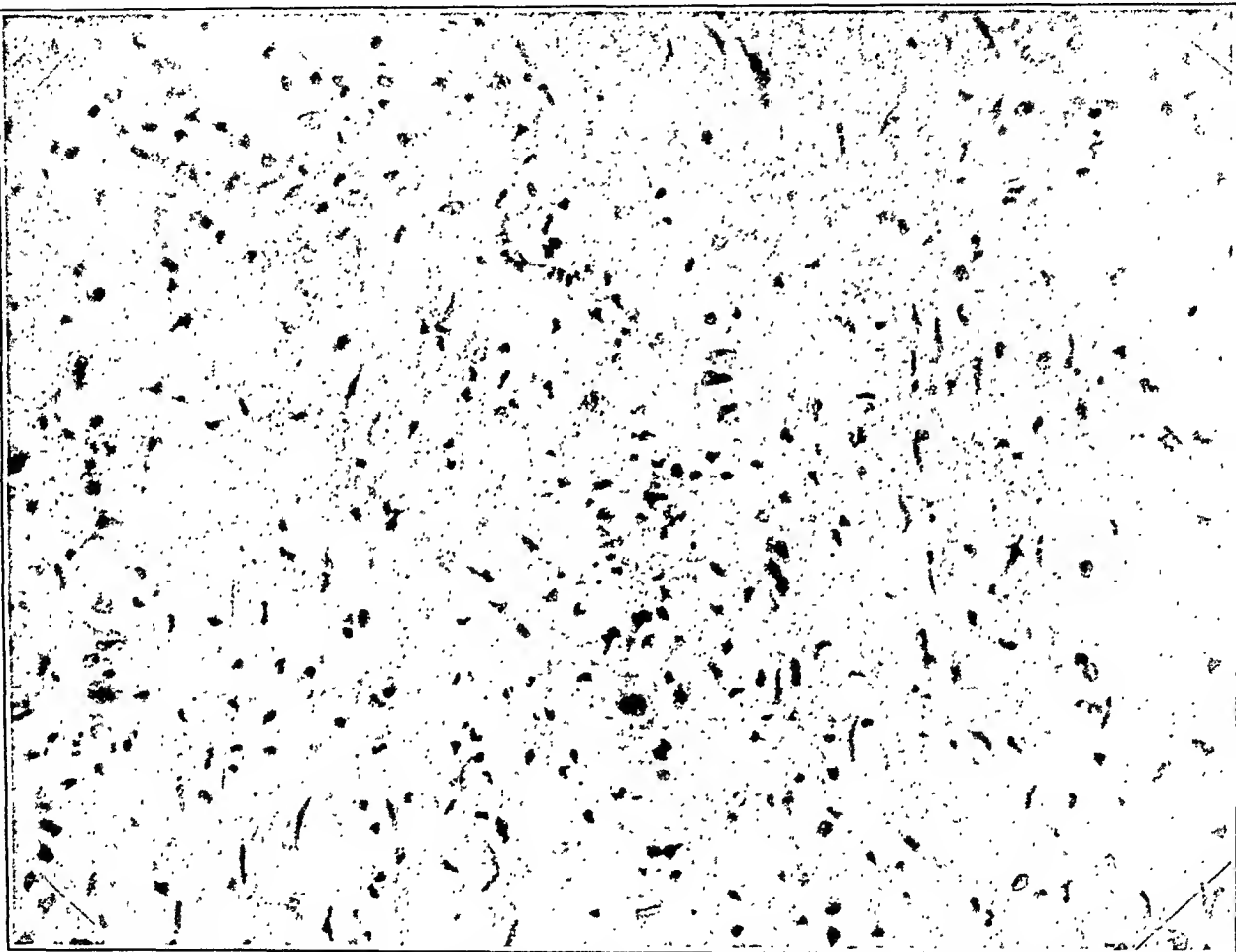


Fig. 12 (case 2).—Photomicrograph of a section of optic nerve, showing loss of the interstitial tissue between the nerve bundles and resulting disorganization of the normal architecture.

only in the earliest lesions; lymphocytes and plasma cells soon predominate, and perivascular lymph spaces packed with these cells (fig. 11) are seen throughout the nerve tissue in a case of neuromyelitis optica. As the process continues, the parenchyma farther from the vessel becomes edematous and begins to degenerate; the same cellular infiltration follows. Degeneration and cellular infiltration of the white matter may be seen between two blood vessels entering the cord; infiltration of the pia-arachnoid by the same cells can also be seen. In

the optic nerves, the interstitial tissue between the nerve bundles is involved very early, and the normal architecture of the nerve disappears (fig. 12).

**Stage of Tissue Destruction:** The first breakdown of nerve tissue is seen in the demyelination of the neurons in this small perivascular focus; figure 13 shows several of these small perivascular foci. In this stage of beginning demyelination, microscopic examination of one of the sections stained for myelin shows irregular swelling, fragmentation and partial loss of myelin in individual nerve fibers. As the

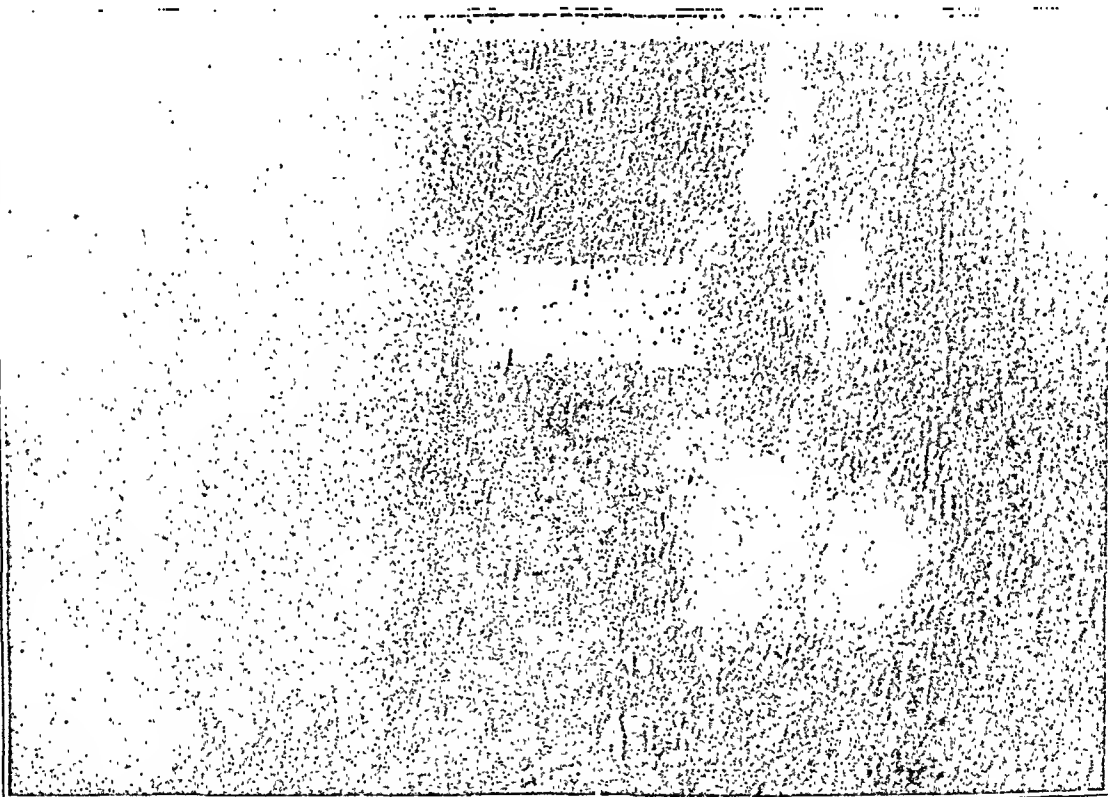


Fig. 13 (case 3).—Photomicrograph of a section of cerebral cortex, showing several small perivascular foci of demyelination and one large coalescent area. Mahon stain.

process continues, the neurons in this original focus become totally demyelinated, and the neurons farther away begin to lose their myelin. A characteristic lesion has a central perivascular core of complete demyelination; outside this is a diffuse zone of partial demyelination with some sheaths missing, some disintegrating sheaths and intact sheaths here and there. The margins of the lesion show a greater number of intact sheaths and fewer sheaths undergoing disintegration. Figure 14 illustrates these zones in a lesion of the optic nerve. The degree of demyelination varies directly with the severity of the proc-

ess; advanced lesions are recognized by the complete lack of staining with the myelin stains, while milder lesions contain numbers of neurons with intact sheaths passing through the softened area (fig. 14). The foci of demyelination vary greatly in size; often, large demyelinated areas cover the entire anterior or lateral white column in the spinal cord or the whole cross section of an optic nerve. On the other hand, there are always small, circumscribed lesions scattered irregularly throughout the spinal cord and optic system. Study of the demyelination explains the formation of the large lesions: As the disease pro-

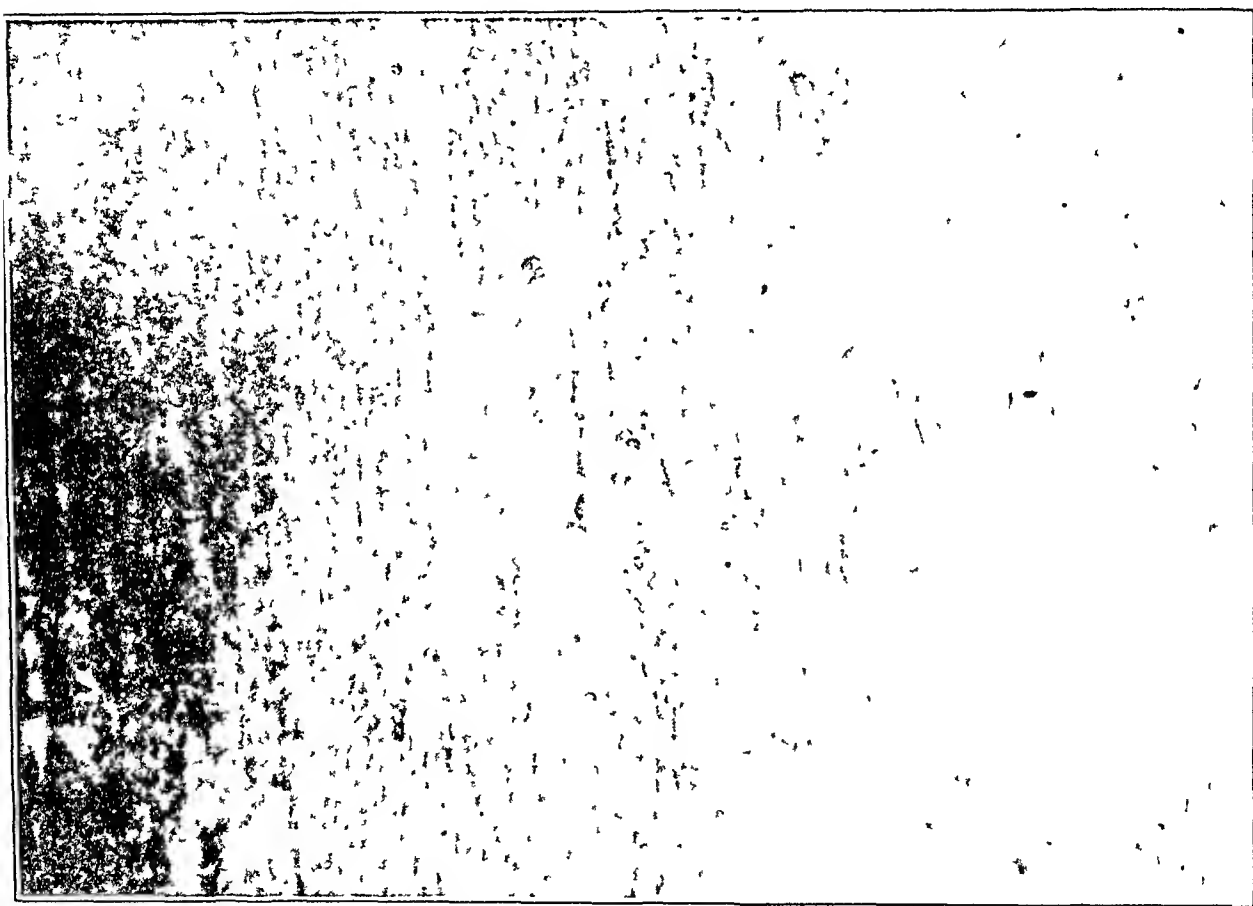


Fig. 14 (case 2).—Photomicrograph of a section of optic nerve, showing the margin of a focus of demyelination. There is almost complete demyelination in the lower right corner, partial loss in the center and little loss of myelin to the left. Weil stain.

gresses, the original small perivascular foci spread out, coalesce and eventually form large, irregular lesions (fig. 13), with no obvious relation to blood vessels.

When the process is mild, the nerves may suffer no more damage than the loss of their myelin sheathing, but when it is severe the axis-cylinders are also destroyed. The latter possibility is the rule in neuromyelitis optica, however, and most lesions (stained appropriately) show edema, fragmentation and disintegration of axis-cylinders micro-



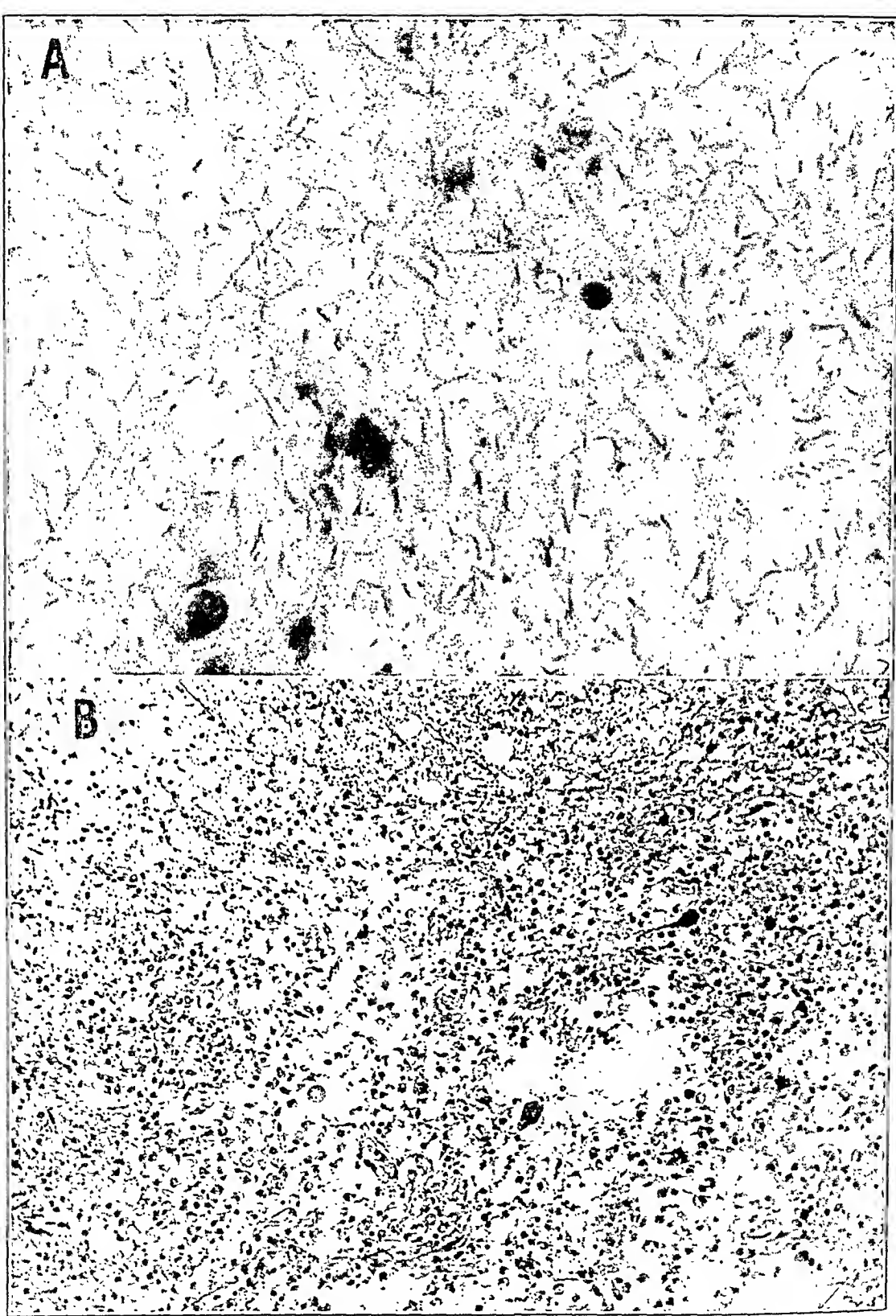


Fig. 15 (case 1).—*A*, photomicrograph of a section of the cord, showing advanced disintegration of axons and a great decrease in number; Bodian stain. *B*, photomicrograph of a section of the anterior gray horn of the cervical portion of the cord, showing more extensive necrosis, with total disappearance of the large nerve cells and clear areas, where all tissue elements have been destroyed.

scopically. The number of destroyed axis-cylinders varies directly with the amount of demyelination; in other words, both factors vary directly with the severity of the process. However, there are always more myelin sheaths lost than axis-cylinders; although many axons are destroyed, a good number are still preserved in the demyelinated foci. Even in the severest lesions, when all myelin sheaths have disappeared, many axis-cylinders are still to be seen. Some of the remaining axons, however, are swollen, distorted and degenerated (fig. 15*A*).

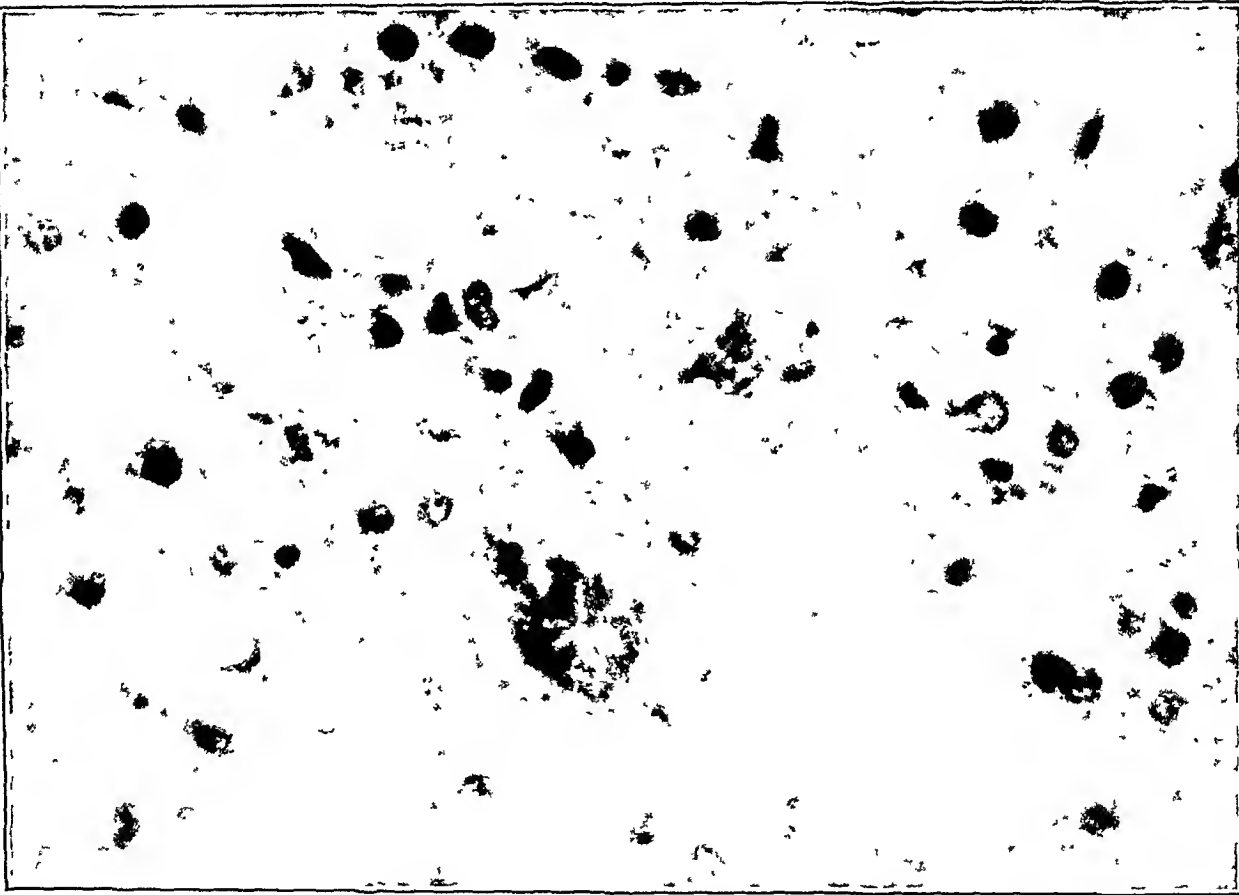


Fig. 16 (case 1).—Photomicrograph of a section of anterior gray horn from the spinal cord, showing advanced necrosis of nerve tissue. A swollen, pyknotic nerve cell is surrounded by the granular remains of interstitial tissue and by phagocytic microglia cells.

The pathology of neuromyelitis optica is not confined to the white matter of the nervous system; the same process, with similar destruction of nerve elements, is also seen in the gray matter. In the spinal cord, foci of destruction are common in the anterior and posterior gray horns. Here the large nerve cells become edematous and undergo chromatolysis. Their neurofibrils break up and agglutinate; there is solution of their Nissl substance. The abundant cytoplasm of these cells becomes fenestrated and vacuolated; the nucleus shrivels and disappears. Pyknosis and neuronophagia are seen; and the cell body

frequently becomes filled with degenerative lipid material. The end result is a pale-staining, vacuolated shell, usually deformed. When the process is toxic enough, complete disintegration and disappearance of the cell body occur (fig. 15 *B*). That this disease is not limited to the white matter is seen in the fact that lesions do not end at the junction of the white and the gray matter. Lesions in the white columns that happen to be located near the central gray matter often protrude into the gray substance or appear to send tongues of necrosis

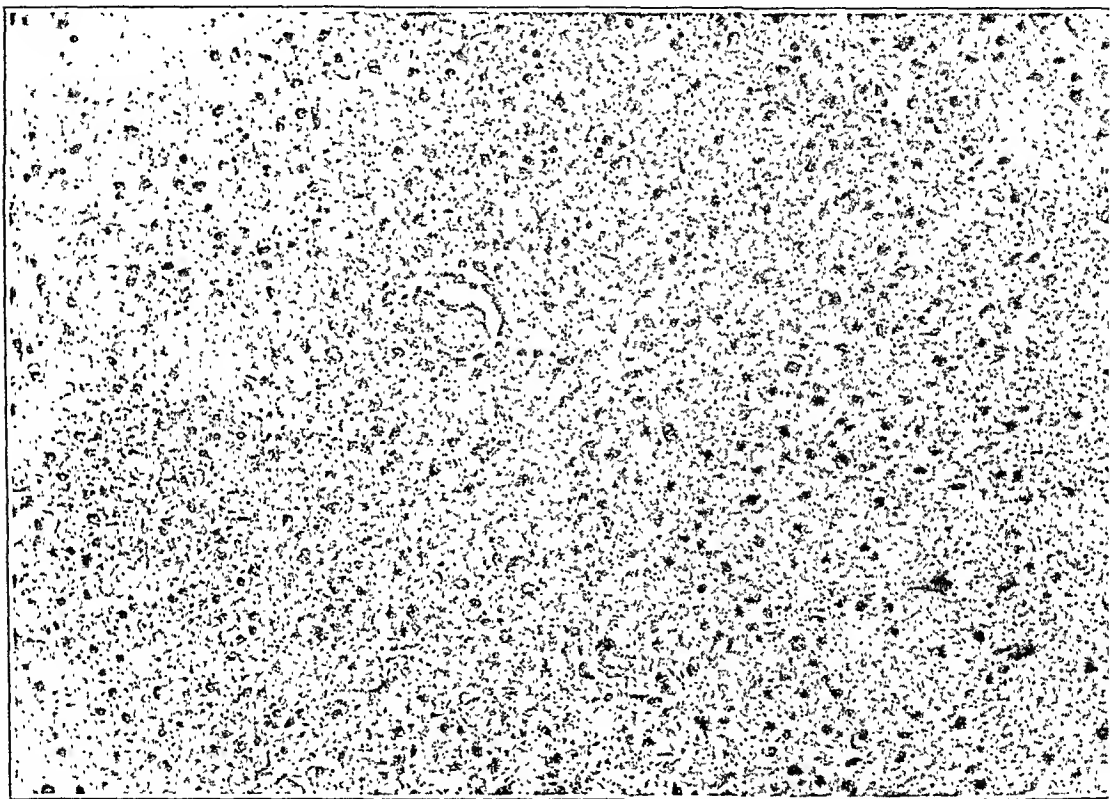


Fig. 17 (case 3).—Photomicrograph of a section of optic nerve, showing a collection of microglia cells in the process of multiplication and proliferation.

into the gray horns. Similarly, lesions situated initially in the central gray matter often bulge out into one of the encircling white columns.

The death of cells constitutes necrosis, and this is the end result in the lesions of neuromyelitis optica, when nerve cell bodies, axis-cylinders, myelin sheaths and interstitial tissue are destroyed. In these necrotic lesions, all degrees of destruction can be seen: fragmentation and disintegration of axons, globules of broken-down myelin, dying nerve cells and remnants of interstitial tissue. Degenerating astrocytes show clasmatodendrosis, and corpora amylacea, from hyalinization of astrocytes, are to be noted. The "scavenging" microglia cells, hyper-

trophied into fat-granule bodies, are everywhere ingesting fragments of myelin. Figure 16 is a highly magnified photomicrograph of severe necrosis in an anterior gray horn, showing the disintegrated granular remains of interstitial tissue, a swollen pyknotic nerve cell and phagocytic microglia cells. When necrosis occurs in tissue unable to replace the void by scar formation, or when it happens too fast for scarring, loss of substance is the inevitable result. As this vacuolation proceeds, the tissue assumes a cystic appearance. Finally, when microcystic

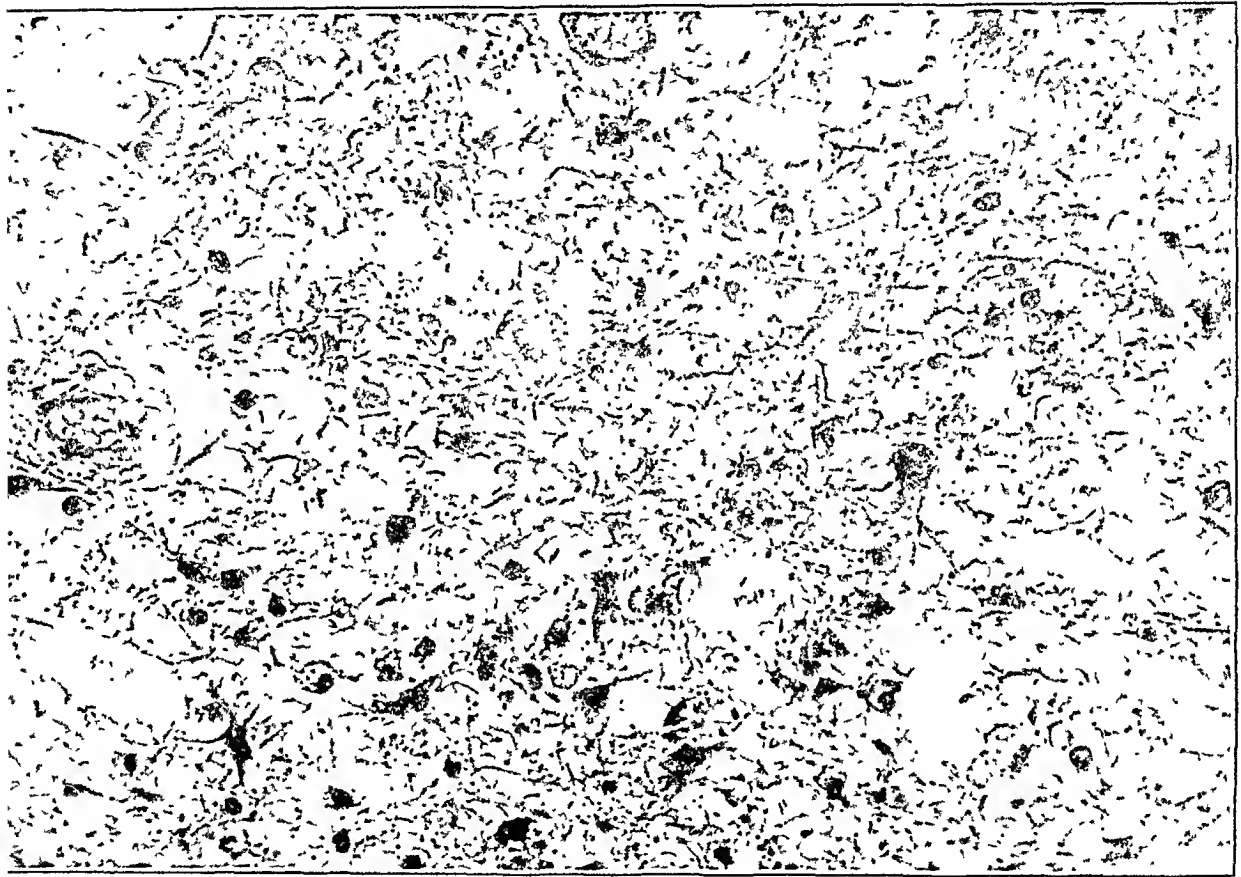


Fig. 18 (case 3).—Photomicrograph of a section of brain stem, showing proliferation of astrocytes in a degenerated area.

degeneration becomes severe enough and extensive enough, gross cavitation results, as seen in the spinal cord in case 5 (fig. 10).

Stage of Phagocytosis: The first response of the nervous system to this destructive process is the proliferation of the microglia. The microglia cells, considered by some to be part of the reticuloendothelial system, are mesodermal in origin; they are the counterpart of histiocytes in other parts of the body. The microglia cells multiply and hypertrophy, and when seen in collected masses at this stage (fig. 17) they resemble collections of phagocytes in any organ. They now constitute the actively mobile phagocytic cells of the central nervous system. The microglia cells now assume their scavenger function and ingest

myelin globules from the disintegrating myelin sheaths. They are now known as compound granule cells, fat-granule cells or glitter cells. These lipid-laden cells are characteristically seen in large numbers throughout the sections in cases of neuromyelitis optica. The microglia cells also phagocytose the degenerating astrocytes (clasmotodendrosis), the necrotic nerve cells (neuronophagia) and the remnants of the axons.

Healing Stage: The second response of the nerve tissue in neuromyelitis optica is a poor attempt at repair; this consists first of multiplication and hypertrophy of astrocytes (fig. 18). The astrocytes are

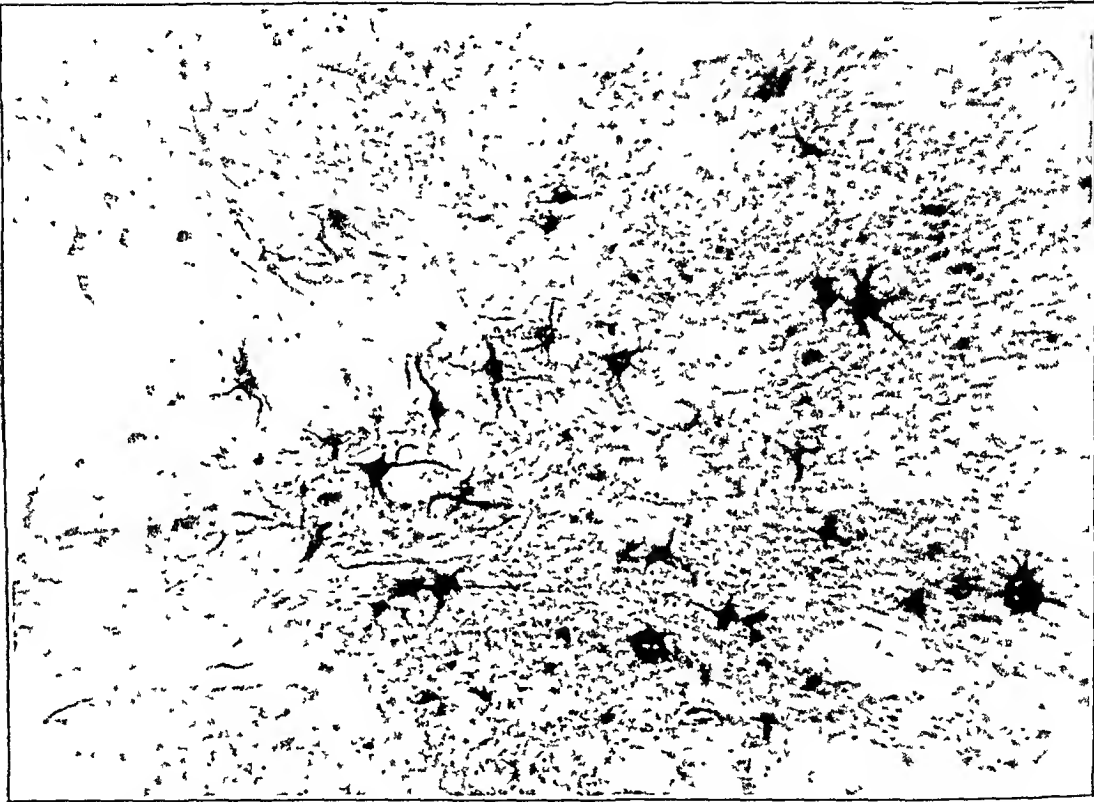


Fig. 19 (case 4).—Photomicrograph of a section of the right optic nerve, showing a group of astrocytes in an old inactive lesion.

the connective tissue cells of the central nervous system; they form the framework for the nerve tissue. Astrocytes may be compared to the cells of Müller in the retina; their cell bodies, likewise, lie within the stroma of the tissue and send out filamentous processes, with a foot plate at the termination, inward to form the internal limiting membrane of the central canal and ventricles and outward to form the external limiting membrane of the neuraxis. Because astrocytosis is reparative and secondary, and is seen after the subsidence of the acute inflammatory reaction, it is not prominent in the lesions of neuromyelitis optica, in which the patient usually dies in the acute stage of

the disease. In the early lesions, few or no astrocytes may be found; when they are seen, they are in the periphery of the necrotic area or in the healthy tissue just outside the lesion. (The normal complement of astrocytes at the site of a lesion are destroyed, with the other tissue elements.) In the older lesions, they are more prominent (fig. 19) as they grow into the necrotic focus to help the healing process, but astrocytes are never seen in great numbers as are the microglia.

The final reaction of the nervous system to the noxae of neuromyelitis optica is gliosis or scarring, by means of fibers laid down by

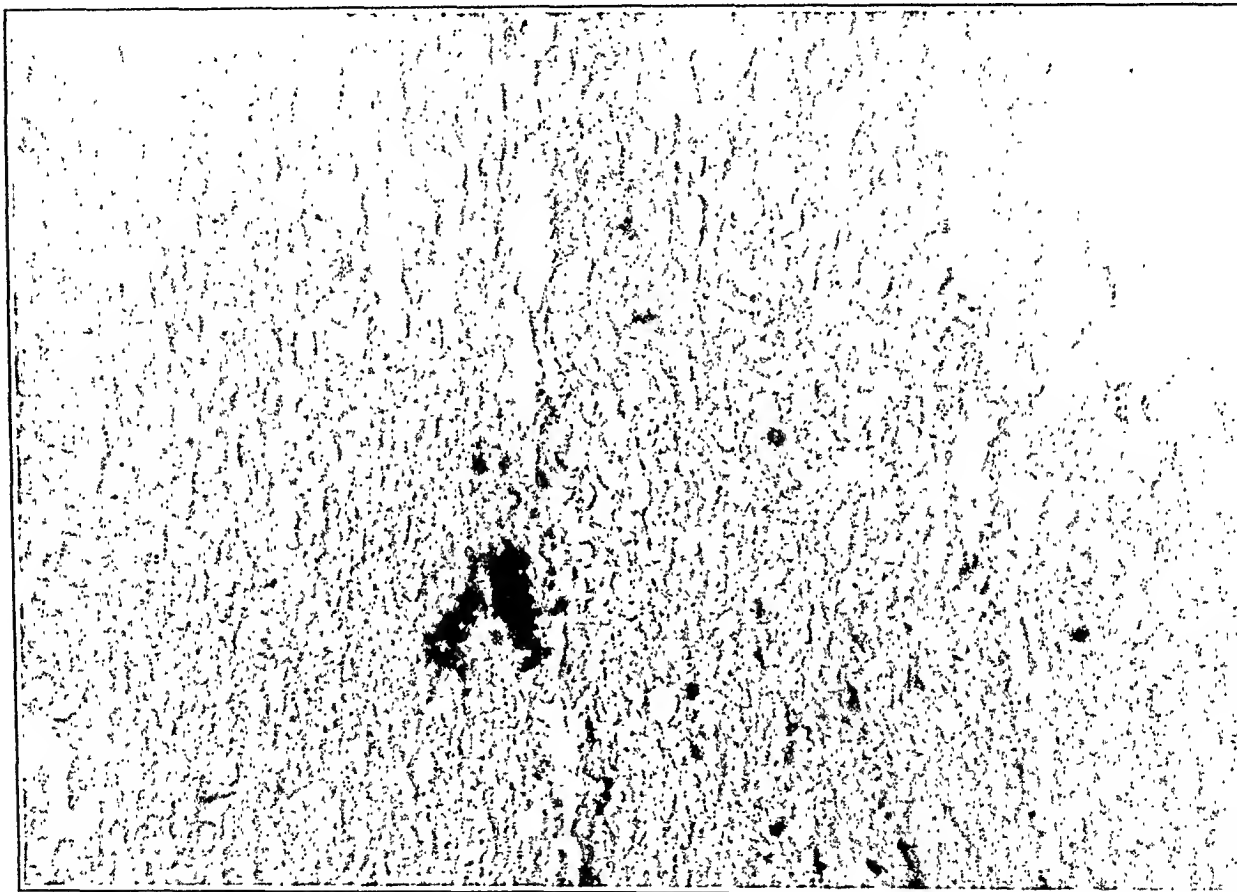


Fig. 20 (case 2).—Photomicrograph of a section of optic nerve, showing fairly dense gliosis.

the astrocytes. This is the connective tissue scar of the nerve tissue. It is seldom observed in this disease, and then only as partially formed glial scars. In 1 case of this study, however, a well developed scar was exhibited in one optic nerve (fig. 20).

#### ETIOLOGY

The earliest writers on neuromyelitis optica attempted to associate the optic neuritis with the pathologic process in the spinal cord by direct extension. Jones <sup>71</sup> hypothesized that injury to the spinal cord

71. Jones, W., cited by Allbutt.<sup>2</sup>

may involve the sympathetic nerves at their origin in the cervical segments and that the resulting irritation interferes with the vascular supply to the eye. Rieger and Forster<sup>11d</sup> elaborated Jones's theory, stating that the vasomotor paralysis produces first hyperemia and then atrophy of the optic nerves. Other investigators of that period, among them Allbutt,<sup>2</sup> concluded that optic neuritis following myelitis is caused by an ascending meningitis. Achard and Guinon<sup>6</sup> indicated alcohol as the cause in their case, as did Fuchs<sup>8n</sup> in his case. Dreschfeld<sup>11i</sup> stated the opinion that in most cases the condition follows the acute infectious diseases. Katz<sup>11n</sup> concluded that syphilis was the cause in 5 of the 15 cases he collected; in the remainder he attributed the disease to a poison with an affinity for the optic nerves and spinal cord. Cobbledick<sup>72</sup> attributed the disease in his case definitely to syphilis, and more recently Milian and associates<sup>38</sup> and Schaeffer<sup>73</sup> have stated that syphilis is a factor. Elschnig<sup>11j</sup> was first to suggest a noxious agent transmitted through the blood stream; later, Bielschowsky,<sup>62</sup> Strümpell<sup>74</sup> and Holden<sup>60</sup> endorsed this opinion.

Goulden,<sup>10</sup> impressed with the constancy of the clinical and pathologic picture, concluded that neuromyelitis optica is a specific infectious disease, an opinion with which Holmes,<sup>75</sup> Michaux,<sup>80</sup> Merkel<sup>76</sup> and Sager and Grigoresco<sup>77</sup> concurred. Holmes offered as proof of specific infection the fact that he had seen this syndrome in epidemic form in the British Expeditionary Forces in France in 1917. Jendralski<sup>13h</sup> reported a case in which he attributed the condition to a septic embolus originating from a paranephritic abscess. Raverdino<sup>78</sup> expressed the belief that the ocular complications of the spinal cord disease were due to increased intracranial pressure. Dedimos<sup>79</sup> reported 2 cases of the disease associated with malaria, in 1 of which improvement followed quinine therapy.

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For a number of years, a neurotropic virus was widely accepted as the cause of neuromyelitis optica, as well as of multiple sclerosis. For the former, a virus origin was particularly sponsored by Abelsdorf,<sup>13c</sup> Redliche,<sup>80</sup> Pette,<sup>81</sup> Paton,<sup>59</sup> Milian and associates<sup>33</sup> and Roger and associates.<sup>82</sup> Pette<sup>81</sup> said that optic neuromyelitis is likely to occur in epidemics of lethargic encephalitis and poliomyelitis. Later, Bouchut and Dechaume,<sup>13j</sup> Vedel and Puech<sup>31k</sup> and van Bogaert<sup>31i</sup> claimed that neuromyelitis optica is a part of the syndrome of epidemic encephalitis. The recent popularity of the virus theory is demonstrated by the fact that Hanes,<sup>83</sup> teaching a class of medical students in 1942, exhibited a case of neuromyelitis optica as a typical example of the virus diseases of the nervous system.

During the past decade, the idea has been repeatedly advanced that all the demyelinating diseases constitute a single disease process, with a variable symptomatology, due to different locations of the lesions. This concept arose originally from the similarity of neuromyelitis optica to multiple sclerosis in some cases, and the idea has since been expanded to include the other demyelinating diseases. Therefore, in any modern exposition of the etiology of neuromyelitis optica one must at least consider the "demyelinating disease group," the main subdivisions of which are (1) multiple sclerosis, (2) neuromyelitis optica, (3) Schilder's disease and its subdivisions and (4) the acute disseminated encephalomyelitides. At present, there are five principal theories of origin for these diseases.

1. *Infectious Theory*.—This theory was born in 1884 with the suggestion of Marie<sup>84</sup> that multiple sclerosis is caused by an infection of the central nervous system secondary to one of the acute infectious diseases (especially typhoid). Marie's theory, however, was soon forgotten, when Strümpell<sup>85</sup> in 1896 expressed the opinion that multiple sclerosis is due to an inherent tendency of the glia to overgrow and destroy the myelin sheaths; without any substantiation, this dictum was unaccountably accepted as fact for two decades. Then, in 1917,

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80. Redliche, E.: Ueber ein gehäuftes Auftreten von Krankheitsfällen mit den Erscheinungen einer Enzephalomyelitis disseminata, *Monatschr. f. Psychiat. u. Neurol.* **64**:152-184, 1927.

81. Pette, H.: Ueber lokalisierte, unter dem Bilde eines raumbeschränkenden Prozesses verlaufende Spinalmeningitis, *Arch. f. Psychiat.* **74**:631-640, 1925.

82. Roger, H.; Opin, T., and Sedán, J.: Neuropticomyléite aiguë avec précession de légers troubles médullaires, *Rev. d'oto-neuro-opt.* **8**:12-16, 1930.

83. Hanes, F. M.: Neuromyelitis Optica: Deficiency States; Actinomycosis, *Internat. Clin.* **1**:207-215, 1942.

84. Marie, P.: Sclérose en plaques et maladies infectieuses, *Progrès méd.* **12**:287-289, 1884.

85. Strümpell, A.: Zur Pathologie der multiplen Sklerose, *Neurol. Centralbl.* **15**:961-964, 1896.



Kuhn and Steiner<sup>86</sup> announced the discovery of a spirochete (*Spirochaeta argentinensis*) in experimental animals inoculated with the spinal fluid of patients with multiple sclerosis. Subsequently, Siemerling,<sup>87</sup> Büscher,<sup>88</sup> Speer<sup>89</sup> and Schuster<sup>90</sup> claimed to have demonstrated this spirochete in human beings with multiple sclerosis. On the other hand, Birley and Dudgeon,<sup>91</sup> Stevenson<sup>92</sup> and Noguchi and Collins<sup>93</sup> were unable to find the organism, and Lüthy<sup>94</sup> soon showed that these "spirochetes" were only fragments and distortions of impregnated axis-cylinders.

The theory of the virus origin of the demyelinating diseases began in 1913, when Bulloch<sup>95</sup> paralyzed rabbits with injections of spinal fluid from patients with multiple sclerosis and concluded that a filtrable virus was the responsible agent. In 1930 Chevassut<sup>96</sup> and Purves-Stewart<sup>97</sup> announced the isolation of the virus of multiple sclerosis (*Spherula insularis*); they prepared an autogenous vaccine from the virus and reported<sup>98</sup> favorable results from its administration to patients with active multiple sclerosis. However, Lépine and Mollaret<sup>99</sup>

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86. Kuhn, P., and Steiner, G.: Ueber die Ursache der multiplen Sklerose, *Klin. med.* **13**:1007-1009, 1917.

87. Siemerling, E.: Spirochäten im Gehirn eines Falles von multipler Sklerose, *Klin. Wchnschr.* **55**:273-274, 1918.

88. Büscher, J.: Spirochätenbefund bei multipler Sklerose: Ein Beitrag zur Pathogenese, *Arch. f. Psychiat.* **62**:426-440, 1920.

89. Speer, E.: Spirochätenbefund im menschlichen Zentralnervensystem bei multipler Sklerose, *München med. Wchnschr.* **68**:425-426, 1921.

90. Schuster, J.: Ein Fall von multipler Sklerose mit positivem Spirochätenbefund, *Ztschr. f. d. ges. Neurol. u. Psychiat.* **73**:433-436, 1921.

91. Birley, J. L., and Dudgeon, L. S.: A Clinical and Experimental Contribution to the Pathogenesis of Disseminated Sclerosis, *Brain* **44**:154-212, 1921.

92. Stevenson, G. S.: Spirochete Stain in Multiple Sclerosis, *Arch. Neurol. & Psychiat.* **9**:88-89 (Jan.) 1923.

93. Noguchi, H., and Collins, J.: An Experimental Study of Multiple Sclerosis: II. Experimental Results in Animals Inoculated with Blood and Cerebrospinal Fluid; Clinical History and General Discussion, *J. A. M. A.* **81**:2110-2112 (Dec. 22) 1923.

94. Lüthy, F.: Zur Frage der Spirochätenbefunde bei multipler Sklerose, *Ztschr. f. d. ges. Neurol. u. Psychiat.* **128**:290-294, 1930.

95. Bulloch, W. E.: The Experimental Transmission of Disseminated Sclerosis to Rabbits, *Lancet* **2**:1185-1186, 1913.

96. Chevassut, K.: The Etiology of Disseminated Sclerosis, *Lancet* **1**:552-560, 1930.

97. Purves-Stewart, J.: A Specific Vaccine Treatment in Disseminated Sclerosis, *Lancet* **1**:560-564, 1930.

98. Purves-Stewart, J.: Disseminated Sclerosis: Experimental Vaccine Treatment, *Lancet* **1**:1072-1073, 1930.

99. Lépine, P., and Mollaret, P.: Recherches sur l'étiologie de la sclérose en plaques, *Bull. Acad. de méd., Paris* **105**:512-518, 1931.

and Tronconi<sup>100</sup> immediately reported the observation of this spherule in the spinal fluid in other diseases. Hicks and Hocking<sup>101</sup> repeated Chevassut's work and concluded that the spherule was not a virus but a precipitation phenomenon found in many other conditions. The virus theory has not been discarded, however, and reports of the isolation of the virus still appear in the literature.<sup>102</sup>

The infectious theory of causation has received support from the fact that acute disseminated encephalomyelitis following various infectious diseases (measles, scarlet fever, chickenpox) and certain prophylactic measures (the Pasteur treatment, administration of tetanus antitoxin) possesses a demyelinating process similar to that of multiple sclerosis and neuromyelitis optica. Clinically, the significant fact is that the encephalitis occurs late in the course of a virus disease; this has, of course, led many to think that the encephalitis is a manifestation in the nervous system of the virus producing the initial disease. Attempts to recover the virus from the nerve tissue, however, have been unsuccessful. It has also been observed that this encephalitis occasionally follows a disease not caused by a virus, and this observation led to the proposal that an unknown neurotropic virus is activated by many diseases, but especially by virus diseases. The fact remains, however, that no virus has yet been demonstrated that will produce the typical demyelinating lesion, either in man or in an experimental animal (Rivers,<sup>103</sup> Hurst<sup>10</sup>).

2. *Toxic Theory*.—Over fifty years ago, Oppenheim,<sup>104</sup> noting that some of his patients with multiple sclerosis were exposed occupationally to lead intoxication, attributed the lesions of that disease to lead as a toxic substance. This hypothesis was revived in 1932, when Hallervorden<sup>105</sup> compared the concentric rings of demyelination of Baló<sup>106</sup> with the Liesegang chemical phenomenon and suggested that multiple sclerosis may similarly be caused by the diffusion of a toxin

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100. Tronconi, V.: Sulla etiologica della sclerosi in placche: Ricerche sulla cosiddetta "spherula insularis," Boll. Soc. med.-chir., Pavia **45**:355-359, 1931.

101. Hicks, J. A. B., and Hocking, F. D. M.: Observations on a Spherule Recently Described in Disseminated Sclerosis, Lancet **2**:401-402, 1931.

102. Margulis, M. S.; Soloviev, V. D., and Shubladze, A. K.: Etiology and Pathogenesis of Acute Sporadic Disseminated Encephalomyelitis and Multiple Sclerosis, J. Neurol., Neurosurg. & Psychiat. **9**:63-74, 1946.

103. Rivers, T. M.: Relation of the Filtrable Viruses to Diseases of the Nervous System, Arch. Neurol. & Psychiat. **28**:757-777 (Oct.) 1932.

104. Oppenheim, H.: Zur Lehre von der multiplen Sklerose, Klin. Wchnschr. **33**:184-189, 1896.

105. Hallervorden, J.: Zur Pathogenese der multiplen Sklerose und ein Vorschlag zur Therapie, München. med. Wchnschr. **79**:602-604, 1932.

106. Baló, J.: Encephalitis Periaxialis Concentrica, Arch. Neurol. & Psychiat. **19**:242-264 (Feb.) 1928.

from a central point in the brain (lateral ventricles). Clinically, the toxic theory has been supported by reports of demyelination produced by various toxic agents: carbon monoxide (Hilpert<sup>107</sup>), lead (Cone, Russel and Harwood<sup>15</sup>), cadmium (Hadden<sup>108</sup>) and arsenic (Ecker and Kernohan<sup>109</sup>). Experimentally, demyelinated lesions have been produced in laboratory animals by a number of toxic substances: tetanus toxin (Claude,<sup>110</sup> Putnam<sup>111</sup>), saponin (Donaggio<sup>112</sup>), cobra venom and streptococcalysin (Weil<sup>113</sup>), carbon monoxide (Putnam and associates,<sup>114</sup> and Yant and associates<sup>115</sup>), bile (Weil and Crandall<sup>116</sup>) and potassium cyanide (Ferraro,<sup>117</sup> Hurst<sup>118</sup>).

3. *Lipolytic Theory*.—That multiple sclerosis is caused by an enzyme that destroys lecithin was first suggested by Marburg<sup>119</sup> in 1906. In 1930 Brickner<sup>120</sup> investigated this theory in the laboratory; he found that plasma from patients with multiple sclerosis causes

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107. Hilpert, P.: Kohlenoxydvergiftung und multiple Sklerose, Arch. f. Psychiat. **89**:117-130, 1929.

108. Hadden, S. B., in discussion on Lowenberg, K.; DeJong, R. N., and Foster, D. B.: Neuromyelitis Optica: Its Relation to Progressive Necrosis of Spinal Cord and Acute Multiple Sclerosis, Tr. Am. Neurol. A. **67**:59-66, 1941.

109. Ecker, A. D., and Kernohan, J. W.: Arsenic as a Possible Cause of Subacute Encephalomyelitis, Arch. Neurol. & Psychiat. **45**:24-43 (Jan.) 1941.

110. Claude, H.: Myélite expérimentale sub-aiguë par intoxication tétanique, Arch. physiol. norm. et path. **9**:843-847, 1897.

111. Putnam, T. J.: Acute Multiple Sclerosis in Dogs, Arch. Neurol. & Psychiat. **24**:640-641 (Sept.) 1930.

112. Donaggio, A.: Sur le parkinsonisme post-encéphalitique: une doctrine corticonigrique, Rev. neurol. **43**:1058-1059, 1925.

113. Weil, A.: The Effect of Hemolytic Toxins on Nervous Tissue, Arch. Path. **9**:828-842 (April) 1930.

114. Putnam, T. J.; McKenna, J. B., and Morrison, L. R.: Studies in Multiple Sclerosis: I. Histogenesis of Experimental Sclerotic Plaques and Their Relation to Multiple Sclerosis, J. A. M. A. **97**:1591-1596 (Nov. 28) 1931.

115. Yant, W. P.; Chornyak, J.; Schrenck, H. H.; Patty, F. A., and Sayers, R. R.: Studies in Asphyxia, Public Health Bulletin 211, United States Treasury Department, Public Health Service, 1934, p. 61.

116. Weil, A., and Crandall, L. A.: Die Beziehungen zwischen dem Lipasegehalt und der neurotoxischen Wirkung des Serums nach experimenteller Leberschädigung, Ztschr. f. d. ges. Neurol. u. Psychiat. **140**:577-592, 1932.

117. Ferraro, A.: Experimental Toxic Encephalomyelopathy (Diffuse Sclerosis Following Subcutaneous Injections of Potassium Cyanide), Psychiat. Quart. **7**:267-283, 1933.

118. Hurst, W. E.: Experimental Demyelination of the Central Nervous System: I. The Encephalopathy Produced by Potassium Cyanide, Australian J. Exper. Biol. & M. Sc. **18**:201-223, 1940.

119. Marburg, O.: Die sogenannte akute multiple Sklerose, Jahrb. f. Psychiat. **27**:213-312, 1906.

120. Brickner, R. M.: Studies on the Pathogenesis of Multiple Sclerosis, Arch. Neurol. & Psychiat. **23**:715-726 (April) 1930.

demyelination in the spinal cord of rats. Brickner hypothesized an enzymatic lipase as the cause of this disease. Then Brickner<sup>121</sup> tested the lipolytic power of serum from patients with multiple sclerosis to hydrolyze certain esters; he found that the blood serums from these patients shows higher lipolytic activity than normal blood serum and cited this finding as additional proof of his theory. However, Crandall and Cherry<sup>122</sup> showed that this lipase is also obtainable in equal amounts in patients with hepatic disease and, in lesser amounts, in many other conditions. Weil and Cleveland<sup>123</sup> repeated Brickner's experiments and agreed that the serum from patients with multiple sclerosis has an abnormally destructive action on the spinal cord of rats, but they also produced this destruction with serums from patients with other diseases. In 1935 Weil and Luhan<sup>124</sup> demonstrated a myelolytic substance in the urine of patients with multiple sclerosis, but, again, the enzymatic material was found in other conditions.

4. *Theory of Vascular Obstruction.*—That vascular occlusion is a factor in the pathogenesis of multiple sclerosis was suggested long ago (Rindfleisch,<sup>125</sup> Ribbert<sup>126</sup>); but thrombi, when present, have generally been considered one of the secondary changes produced by the disease. In 1928 Meyer<sup>127</sup> claimed priority in the production of demyelinated lesions by means of vascular occlusion. In 1931 Putnam and associates<sup>128</sup> repeated Meyer's experiments and found that a small minority of the animals showed demyelinated lesions surrounding a thrombosed vessel. Putnam<sup>128</sup> stated that the histologic changes produced by obstructive agents were so similar to the lesions of multiple sclerosis

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121. Brickner, R. M.: Studies of the Pathogenesis of Multiple Sclerosis: III. Further Evidence of Abnormal Lipolytic Activity in the Blood in Multiple Sclerosis, *Bull. Neurol. Inst. New York* **2**:119-133, 1932.

122. Crandall, L. A., Jr., and Cherry, I. S.: Presence of an Olive Oil Splitting Lipase in the Blood of Patients with Multiple Sclerosis, *Proc. Soc. Exper. Biol. & Med.* **28**:572-574, 1931; Blood Lipase, Diastase, and Esterase in Multiple Sclerosis, *Arch. Neurol. & Psychiat.* **27**:367-374 (Feb.) 1932.

123. Weil, A., and Cleveland, D. A. A.: A Serologic Study of Multiple Sclerosis, *Arch. Neurol. & Psychiat.* **27**:375-388 (Feb.) 1932.

124. Weil, A., and Luhan, J. A.: The Demonstration of Myelolytic Substances in the Urine of Patients with Disseminated Sclerosis, *Arch. Neurol. & Psychiat.* **34**:459-461 (Aug.) 1935.

125. Rindfleisch, E.: Histologisches Detail zu der graven Degeneration von Gehirn und Rückenmark, *Virchows Arch. f. path. Anat.* **26**:474-483, 1863.

126. Ribbert, H.: Ueber multiple Sklerose des Gehirns und Rückenmarks, *Virchows Arch. f. path. Anat.* **90**:243-260, 1882.

127. Meyer, A.: Experimentelle Erfahrungen über die Kohlenoxydvergiftung des Zentralnervensystems, *Ztschr. f. d. ges. Neurol. u. Psychiat.* **112**:187-212, 1928.

128. Putnam, T. J.: Studies in Multiple Sclerosis: IV. "Encephalitis" and Sclerotic Plaques Produced by Venular Obstruction, *Arch. Neurol. & Psychiat.* **33**:929-940 (May) 1935.

that venular obstruction must be an essential antecedent to plaque formation. Later, Putnam<sup>129</sup> claimed to have demonstrated thrombi in human cases of encephalitis and multiple sclerosis and concluded that the primary factor in these diseases is to be found in the clotting mechanism of the blood. In 1943 Scheinker<sup>130</sup> studied the pathologic collection at the Salpêtrière and corroborated Putnam's hypothesis of plaque formation about small venous thromboses.

On the other hand, Dattner<sup>131</sup> found that the clotting time of the blood was lengthened in many cases of multiple sclerosis. Dow and Berglund<sup>132</sup> in 1942, in a meticulous study of serial sections of 60 plaques, noted no signs of thrombosis in 51 of the lesions; in the remaining 9 lesions the observations were indecisive. These authors expressed doubt that thrombi sufficiently large to produce these plaques could disappear without a trace. In 1946 Reese,<sup>133</sup> reporting the use of an anticoagulant drug, dicumarol® (3,3-methylenebis 4-hydroxycoumarin), in 28 cases of multiple sclerosis, found no objective improvement in any of his cases.

Recently, Franklin and Brickner<sup>134</sup> suggested that the lesions of multiple sclerosis are caused by vasospasm of the smaller arterial vessels. Studying the retinal arterioles in 18 patients with this disease, they found scotomas associated with arteriolar constrictions and were able to reduce both the constrictions and the size of the scotomas with vasodilators. Franklin and Brickner could not explain the cause of the vasospasms.

5. *Allergic Theory*.—The allergic theory for the demyelinating diseases evolved from the persistent reports in the literature of encephalitis, encephalomyelitis and myelitis following the administration of various serums and vaccines, especially vaccination and the Pasteur treatment.

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129. Putnam, T. J.: Evidences of Vascular Occlusion in Multiple Sclerosis and "Encephalomyelitis," *Arch. Neurol. & Psychiat.* **37**:1298-1321 (June) 1937. Putnam, T. J., and Alexander, L.: Disseminated Encephalomyelitis: A Histologic Syndrome Associated with Thrombosis of Small Cerebral Vessels, *ibid.* **41**:1087-1110 (June) 1939.

130. Scheinker, I. M.: Histogenesis of the Early Lesions of Multiple Sclerosis, *Arch. Neurol. & Psychiat.* **49**:178-185 (Feb.) 1943.

131. Dattner, B.: Pathogenesis of Multiple Sclerosis, *Arch. Neurol. & Psychiat.* **37**:1221 (June) 1937.

132. Dow, R. S., and Berglund, G.: Vascular Pattern of Lesions of Multiple Sclerosis, *Arch. Neurol. & Psychiat.* **47**:1-18 (Jan.) 1942.

133. Reese, H. H.: What Do We Know About Multiple Sclerosis? *Journal-Lancet* **66**:359-362, 1946.

134. Franklin, C. R., and Brickner, R. M.: Vasospasm Associated with Multiple Sclerosis, *Arch. Neurol. & Psychiat.* **58**:125-162 (Aug.) 1947.

Bassoe and Grinker,<sup>135</sup> Gayle and Bowen,<sup>136</sup> Kraus and Chaney,<sup>137</sup> Scheinker<sup>138</sup> and many others have reported encephalomyelitis following immunization procedures. In 1929 Foster Kennedy<sup>139</sup> was the first in this country to draw attention to the occasional encephalopathy following the use of foreign serums. Since that time, Allen,<sup>140</sup> Doyle<sup>141</sup> and Winkelman and Gotten<sup>142</sup> have discussed encephalomyelitis following serum therapy. Glanzmann<sup>143</sup> was first actually to attribute these nervous complications to allergy. This concept was evidently engendered by the fact that a period, approximately comparable to that required for the development of sensitivity to a foreign protein, usually elapses between the administration of the vaccine or serum and the onset of the complicating encephalitis. Kennedy,<sup>144</sup> denying the existence of any proof of the allergic theory, at the same time admitted that the clinical events of these processes in the central nervous system resemble multiple sclerosis and that the pathologic features are also suggestively similar.

In 1937 Ferraro<sup>35</sup> published a comprehensive review of the pathology of the demyelinating diseases, in which he attempted to prove that these diseases are allergic reactions of the nervous system because of the similarity of their pathology to that of experimental anaphylaxis in laboratory animals. Ferraro listed as the essential pathologic features of these conditions (1) perivascular demyelination, (2) hemorrhages, (3) degeneration of the walls of the blood vessels, (4) thrombus formation, (5) perivascular cellular infiltration, (6) giant cells, (7) necrosis and (8) gliosis. According to Ferraro, interpretation of this pathologic

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135. Bassoe, P., and Grinker, R. R.: Human Rabies and Rabies Vaccine Encephalomyelitis, *Arch. Neurol. & Psychiat.* **23**:1138-1160 (April) 1930.

136. Gayle, R. F., and Bowen, R. H.: Acute Ascending Myelitis Following the Administration of Typhoid Vaccine: Report of a Case with Necropsy Findings, *J. Nerv. & Ment. Dis.* **78**:221-231, 1933.

137. Kraus, W. M., and Chaney, L. B.: Serum Disease of the Nervous System, *Arch. Neurol. & Psychiat.* **37**:1035-1047 (May) 1937.

138. Scheinker, I. M.: Disseminated Encephalomyelitis and Its Relation to Multiple Sclerosis, *J. Neuropath. & Exper. Neurol.* **2**:418-419, 1943.

139. Kennedy, F.: Certain Nervous Complications Following the Use of Therapeutic and Prophylactic Sera, *Am. J. M. Sc.* **177**:555-559, 1929.

140. Allen, I. M.: The Neurological Complications of Serum Treatment, *Lancet* **2**:1128-1131, 1931.

141. Doyle, J. B.: Neurologic Complications of Serum Sickness, *Am. J. M. Sc.* **185**:484-492, 1933.

142. Winkelman, N. W., and Gotten, N.: Encephalomyelitis Following the Use of Serum and Vaccine, *Am. J. Syph. & Neurol.* **19**:414-424, 1935.

143. Glanzmann, E.: Die nervösen Komplikationen der Varizellen, Variola, und Vakzine, *Schweiz. med. Wchnschr.* **57**:145-154, 1927.

144. Kennedy, F.: Allergy and Its Effects on the Central Nervous System, *J. Nerv. & Ment. Dis.* **88**:91-100, 1938.

change as an allergic reaction does not exclude the thrombus theory of Putnam; the basic process may be an allergic thrombus formation. In addition to thrombosis, Ferraro stated that allergy may cause vascular obstruction by vasospasm, by changing the coagulation time of the blood and by causing periarteritis or intimal hyperplasia.

Finley<sup>145</sup> in 1938 discussed allergy as a factor in the encephalitis associated with vaccination, variola and measles; he recalled that the expanding vaccinia reaction (eighth to twelfth days) represents the reaction between antibodies then forming and the virus in the papule. According to Finley, this reaction occurs all over the body, giving rise to local or general exanthems (if they occur) at this time, and also to the cerebral complications in about 90 per cent of cases. He concluded that the nervous complications represent an allergic response of nervous system to the virus of the exanthem. Baer and Sulzberger,<sup>146</sup> stating the belief that the allergic theory is based on circumstantial evidence, looked for another common form of allergy, atopic hypersensitivity, in 40 cases of multiple sclerosis. They were able to demonstrate it in only 10 cases, an incidence they considered not significantly higher than that in the general population.

Experimental Evidence for the Allergic Theory: First, it was obvious that the demonstration of brain-specific antigens was necessary to the hypothesis of encephalopathy caused by an antigen-antibody reaction. This proof was accomplished by Heimann and Steinfeld<sup>147</sup> and Plaut and Kassowitz<sup>148</sup> twenty years ago; these workers found that heterologous brain tissue was specific when injected into rabbits. Normal homologous brain is not antigenic, but Schwentker and Rivers<sup>149</sup> showed that autolysis or disease (vaccination) may so alter the tissues as to render them antigenic. Rivers and Schwentker<sup>150</sup>

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145. Finley, K. H.: Pathogenesis of Encephalitis Occurring with Vaccination, Variola and Measles, *Arch. Neurol. & Psychiat.* **39**:1047-1054 (May) 1938.

146. Baer, R. L., and Sulzberger, M. B.: Role of Allergy in Multiple Sclerosis: Incidence of Atopy in a Series of Forty Cases, *Arch. Neurol. & Psychiat.* **42**:837-841 (Nov.) 1939.

147. Heimann, F., and Steinfeld, J.: Ueber das Verhalten der Hirnlipoide und ihrer Antisera, *Ztschr. f. Immunitätsforsch. u. exper. Therap.* **58**:181-192, 1928.

148. Plaut, F., and Kassowitz, H.: Ueber die Entstehung von Hirnantikörpern bei der Immunisierung normaler und syphilitischer Kaninchen mittels Hirnsuspensionen, *Ztschr. f. Immunitätsforsch. u. exper. Therap.* **63**:428-439, 1929.

149. Schwentker, F. F., and Rivers, T. M.: The Antibody Response of Rabbits to Injections of Emulsions and Extracts of Homologous Brain, *J. Exper. Med.* **60**:559-574, 1934.

150. Rivers, T. M., and Schwentker, F. F.: Encephalomyelitis Accompanied by Myelin Destruction Experimentally Produced in Monkeys, *J. Exper. Med.* **61**:689-702, 1935.

then produced demyelinated lesions in monkeys with extracts of rabbit brain. Ferraro and Jervis<sup>151</sup> were successful in producing progressive neurologic signs in monkeys inoculated with rabbit brain; pathologically, they demonstrated lesions somewhat similar to those of the demyelinating diseases.

Anaphylaxis, an available laboratory procedure, has also been investigated for elucidation of any relation between allergy and the demyelinating diseases; similarity of the pathology of the Arthus phenomenon opened an easy avenue for laboratory exploration. Davidoff and associates<sup>152</sup> produced sensitivity in the brains of rabbits and then demonstrated local anaphylaxis of brain tissue at the site of antigen inoculation that was similar to the Arthus phenomenon seen in the skin. Kopeloff and associates<sup>153</sup> produced fatal anaphylaxis at will in monkeys by employing larger doses of the antigen. Alexander and Campbell<sup>154</sup> have demonstrated the Arthus phenomenon in the brains of guinea pigs. Using Forssman antibodies that cause demonstrable damage to capillaries, Jervis<sup>155</sup> produced demyelinated lesions about damaged capillaries in guinea pig brains and claimed that he had produced demyelinated lesions at the site of an antigen-antibody reaction. Other investigators have been unable to produce these demyelinated lesions; Dechaume and Croizat,<sup>156</sup> Garcin and Bertrand,<sup>157</sup> Baginski and associates<sup>158</sup> and Stief and Tokay<sup>159</sup> have all described anaphylactic lesions in the nervous system, in none of which demyelination appeared to be a feature.

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151. Ferraro, A., and Jervis, G. A.: Experimental Disseminated Encephalopathy in the Monkey, *Arch. Neurol. & Psychiat.* **43**:195-209 (Feb.) 1940.

152. Davidoff, L. M.; Seegal, B. C.; and Seegal, D.: The Arthus Phenomenon: Local Anaphylactic Inflammation in the Rabbit Brain, *J. Exper. Med.* **55**: 163-168, 1932.

153. Kopeloff, N.; Davidoff, L. M., and Kopeloff, L.: General and Cerebral Anaphylaxis in the Monkey (*Macacus Rhesus*), *J. Immunol.* **30**:477-485, 1936.

154. Alexander, L., and Campbell, A. C. P.: Local Anaphylactic Lesions of the Brain in Guinea Pigs, *Am. J. Path.* **13**:229-248, 1937.

155. Jervis, G. A.: Forssman's "Carotid Syndrome": A Contribution to the Study of Anaphylactic Changes in the Nervous System from the Standpoint of Pathology, *Arch. Path.* **35**:560-570 (April) 1943.

156. Dechaume, J., and Croizat, P.: Lésions nerveuses dans l'anaphylaxie chronique expérimentale, *Compt. rend. Soc. de biol.* **101**:1145-1146, 1929.

157. Garcin, R., and Bertrand, I.: Étude expérimentale des lésions du névraxe consécutives aux chocs anaphylactiques répétés et aux injections répétitives espacées d'albumine étrangère: Sur quelques considérations pathogéniques applicables à la neuro-pathologie humaine, *Bull. et mém. Soc. méd. d. hôp. de Paris* **51**:787-796, 1935.

158. Baginski, S.; Czarnecki, E., and Hurynawicz, J.: Lésions histologiques du système nerveux des lapins en état anaphylactiques, *Compt. rend. Soc. de biol.* **130**:567-569, 1939.

159. Stief, A., and Tokay, L.: Durch experimentelle Serumanaphylaxie verursachte Veränderungen des Nervensystems, *Ztschr. f. d. ges. Neurol. u. Psychiat.* **150**:715-728, 1934.



*Comment.*—1. The infectious theory, the oldest and most popular, has never been substantiated. The spirochetal hypothesis has been abandoned. Chevassut's organism has been discredited. The virus theory still has many proponents and remains a definite possibility. Against the virus theory is the argument that none of the known neurotropic viruses produce the demyelinating type of lesion.

2. The evidence in favor of the toxic theory appears weak. A few cases of multiple sclerosis and neuromyelitis optica have been found in association with poisoning by lead, arsenic and other metals. However, such cases are rare occurrences in the total number of such intoxications, and no relation in these instances has ever been proved except that of coincidence. The production of experimental demyelination by means of toxic substances is invalidated by the questionable similarity of the lesions to the pathologic process in man and by the fact that similar lesions are produced by so many other, nontoxic, agents.

3. The enzyme hypothesis of Brickner has not been accepted. His laboratory procedures and his interpretation of results have been criticized. Other investigators have shown that similar enzymatic substances are present in a number of other diseases.

4. The theory of vascular obstruction advocated by Putnam rests on his claims that he has produced "multiple sclerosis" in animals by occlusion of blood vessels, and that he has consistently demonstrated vascular thromboses in the lesions in man. The main arguments against these claims are (1) the failure of other pathologists to find the thromboses in cases of human multiple sclerosis, (2) the fact that Putnam's experimental lesions are not accepted as similar to the human type, (3) the demonstration of increased clotting time in multiple sclerosis and (4) the failure of anticoagulant therapy clinically.

5. The allergic theory of Ferraro depends on the production of similar lesions in laboratory animals by experimental anaphylaxis, and on the fact that acute encephalomyelitis occasionally follows the administration of serums and vaccines. Opposed to this view are these facts: (1) Many workers have been unable to reproduce Ferraro's results; (2) the experimental lesions do not closely resemble the lesions in man; (3) similar demyelinating lesions are also produced by many other, nonallergic, agents, and (4) the acute encephalomyelitides are not very common in view of the millions of vaccinations and serum injections.

It appears that the importance of demyelination is being overstressed in the search for the cause of the demyelinating diseases. Study of the literature concerning experimental demyelination reveals that a great number of widely different stimuli will cause the destruction of myelin

sheaths. Demyelination is, in fact, one of the first reactions of nerve tissue to trauma, and the injury apparently need not be specific. It has been shown that even minute pressure on a nerve will produce permanent demyelination (Denny-Brown and Brenner<sup>160</sup>). This suggests that the production of demyelination under experimental conditions does not necessarily contribute a clue to the etiology of any human disease.

It will be seen that most of the efforts to establish the etiology of the demyelinating diseases fall into three categories: (1) demonstration of the causative agent or process in man (spirochete, virus, enzyme, thromboses); (2) demonstration of the coincidence of a demyelinating disease and another condition (typhoid, lead poisoning, virus infection), and (3) experimental production of similar lesions in laboratory animals (by a wide variety of noxae). Most workers today are striving to attain the last-named goal (reproduction of similar lesions). This appears to be an attempt to prove what may well be a fallacy, because the demonstration of a similar pathologic process will not prove a similar etiologic agent. Pathologists may work out the histologic picture of a disease, but that gives them no license to draw conclusions as to the cause of the process. There are many identical lesions in the field of pathology that may be caused by two or more agents. The central nervous system, particularly, is so constructed that it can react to injury in only a limited number of ways. There are, therefore, only a certain number of pathologic pictures possible, regardless of the number of exciting agents. How, then, can any one agent causing experimental necrosis in the nervous system of animals, similar to the necrosis of neuromyelitis optica and multiple sclerosis, be necessarily indicted as the cause of these diseases? If this were possible, it would furnish a convenient "short-cut" to the satisfaction of Koch's postulates.

#### DIFFERENTIAL DIAGNOSIS

A large majority of physicians who have encountered a case of neuromyelitis optica have considered the syndrome a specific disease. Clinically, the unusual combination of sudden blindness and crippling paraplegia has made this syndrome appear unique. Pathologically, the severity of the lesions both in the optic nerves and in the spinal cord has contributed to the apparent unicity of the disease. It is significant that the men who have studied the disease extensively have favored the idea of specificity; Goulden,<sup>10</sup> Beck,<sup>12</sup> McAlpine,<sup>14</sup> Walsh,<sup>17</sup> Balser,<sup>18</sup> Hassin<sup>20</sup> and Michaux<sup>30</sup> have all expressed that opinion. Nevertheless,

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160. Denny-Brown, D., and Brenner, C.: Lesion in Peripheral Nerve Resulting from Compression by Spring Clip, *Arch. Neurol. & Psychiat.* **52**:1-19 (July) 1944.

the proof that neuromyelitis optica is a specific disease, namely, the demonstration of the causative agent, is lacking.

The similarity between neuromyelitis optica and multiple sclerosis was noted long ago; Dreschfeld<sup>111</sup> in 1894 first called attention to the pathologic likenesses. Symonds<sup>161</sup> was first to insist on the identity of the two conditions; discussing Beck's case in 1927, he stated that it was actually a rapidly progressive case of multiple sclerosis and pathologically identical with a case of multiple sclerosis in which he had done an autopsy a few years before.<sup>162</sup> According to Symonds, the apparent differences between the two conditions are merely variations in acuteness and intensity. This view has become increasingly popular, especially in the United States, where the theory has particularly been espoused by Putnam and Ferraro. These authors and their colleagues have come to the conclusion that all the demyelinating diseases are fundamentally uniform in their basic pathology. They attribute the confusing clinical diversity of these diseases to differences in distribution and severity of the pathologic lesions and to differences in age, resistance and constitution of the patients. In regard to classification, they maintain that only secondary and unimportant features have been used as criteria for splitting the demyelinating diseases into a multitude of clinical and pathologic divisions and subdivisions.

The essential problem in the differential diagnosis of neuromyelitis optica today, then, is the differentiation (if any) of this syndrome from the other demyelinating diseases: (1) multiple sclerosis, (2) the diffuse scleroses and (3) the acute disseminated encephalomyelitides. Until the etiologic agent in these diseases is discovered, clinical and pathologic characteristics constitute the only available basis for discussion.

*Multiple Sclerosis.*—Although the school of Putnam and Ferraro consider neuromyelitis optica and multiple sclerosis as more or less identical, many other investigators have not agreed and have described a number of differentiating features. The following points of differential diagnosis have been accumulated from the literature, and do not necessarily represent my opinion.

Clinical Differences: 1. Course of the Disease: Neuromyelitis optica is an acute, self-limiting disease, ending in death or in recovery in a relatively short period, whereas multiple sclerosis is a chronic, relapsing disease with a slow downhill course. Variability in its course is a characteristic of multiple sclerosis, while the course of neuromyelitis optica is comparatively uniform. Remissions are very common in the former but relatively uncommon in the latter.

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161. Symonds, C. P., in discussion on Beck,<sup>12</sup> 703.

162. Symonds, C. P.: *The Pathological Anatomy of Disseminated Sclerosis*, Brain 47:36-56, 1924.

2. Loss of Vision: Sudden binocular loss of vision is almost pathognomonic of neuromyelitis optica but rare in multiple sclerosis (Brain,<sup>163</sup> McIntyre and McIntyre<sup>164</sup>). The severity of the visual loss in neuromyelitis optica is usually greater than that in multiple sclerosis, in which it is unusual for even one eye to become totally blind and bilateral total blindness is almost unknown.

3. Occurrence in Children: It is almost universally accepted that multiple sclerosis does not occur before puberty (Garrod and associates<sup>165</sup>) whereas neuromyelitis optica is frequently reported in children. Wechsler<sup>166</sup> and Brain<sup>167</sup> suggested that the few published reports of multiple sclerosis in children represent mistaken diagnoses.

4. Nystagmus: This is a most common occurrence in multiple sclerosis (70 per cent of cases, Brain<sup>167</sup>), but all authors agree that it is rare or nonexistent in neuromyelitis optica. The absence of nystagmus was stated to be one of the main differentiating points by Michaux.<sup>30</sup>

5. Colloidal Gold Curve: It is generally accepted that there is a characteristic colloidal gold curve (Merritt<sup>168</sup>) of the spinal fluid in multiple sclerosis, whereas the findings are normal, or at least non-informative, in cases of neuromyelitis optica.

6. Other Clinical Differences: Pain is uncommon in multiple sclerosis while Balser<sup>18</sup> and McAlpine<sup>25</sup> found pain in the extremities and back a common mode of onset in neuromyelitis optica. Balser and others called attention to the fact that mental disturbances, such as euphoria, are frequent in multiple sclerosis but rare in neuromyelitis optica. Walsh<sup>17</sup> and McAlpine<sup>25</sup> cited the relative absence of palsies of the extraocular muscles in the latter disease, as compared with their occurrence in disseminated sclerosis. Hassin<sup>169</sup> mentioned that the tendon reflexes are almost always exaggerated in multiple sclerosis, but that they are diminished or lost, after an initial period of hyperactivity, in neuromyelitis optica.

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163. Brain, W. R.: Critical Review: Disseminated Sclerosis, *Quart. J. Med.* **23**:343-391, 1930.

164. McIntyre, H. D., and McIntyre, A. P.: Prognosis of Multiple Sclerosis, *Arch. Neurol. & Psychiat.* **50**:431-438 (Oct.) 1943.

165. Garrod, A. E.; Batten, F. E.; Thursfield, H., and Paterson, D.: *Diseases of Children*, New York, William Wood & Company, 1929, pp. 753-754.

166. Wechsler, I. S.: *A Textbook of Clinical Neurology*, Philadelphia, W. B. Saunders Company, 1931, pp. 548.

167. Brain, R.: *Diseases of the Nervous System*, London, Oxford University Press, 1947, p. 503.

168. Merritt, H. H.: The Cerebro-Spinal Fluid in Multiple Sclerosis, *Brain* **57**:56-68, 1934.

169. Hassin, G. B., in discussion on Putnam and Forster.<sup>27</sup>

Pathologic Differences: 1. Distribution of the Lesions: The whole central nervous system is commonly involved in the pathologic changes of multiple sclerosis, whereas in neuromyelitis optica the brain and the brain stem are not usually affected. The optic pathways are always involved in the latter disease (by definition), but are never so constantly affected in multiple sclerosis. The cerebellum is commonly involved in multiple sclerosis but seldom in neuromyelitis optica.

2. Involvement of the Gray Matter: Multiple sclerosis is practically limited to the white matter of the nervous system, but the gray substance is impartially involved in the lesions of neuromyelitis optica. Further, Hassin<sup>170</sup> added that when the gray matter is involved in multiple sclerosis the changes are slight and the ganglion cells spared, in contradistinction to the death of nerve cells seen in neuromyelitis optica.

3. Destruction of Axis-Cylinders: Many authors have expressed the opinion that the active phase of multiple sclerosis is restricted to the destruction of myelin sheaths and that the process ends when this is completed. On the other hand, the disintegration of axis-cylinders is a characteristic feature of neuromyelitis optica.

4. Cellular Infiltration: Those who favor the specificity of neuromyelitis optica state that polymorphonuclear leukocytes (early), lymphocytes and plasma cells are noted in great numbers in that disease but that collections of these cells are rare in multiple sclerosis. They also state that perivascular round cell infiltration is widespread throughout the nervous system in neuromyelitis optica, irrespective of the foci of necrosis, and that this is not a feature in multiple sclerosis.

5. Cavitation: Rarefaction of tissue, progressing to gross cavitation, is frequently reported in cases of neuromyelitis optica but never in cases of multiple sclerosis. Lowenberg<sup>171</sup> stated that the abundant proliferation of fibrous glia in multiple sclerosis insures a scar (plaque), so that cavity formation cannot occur.

6. Gliosis: This is seldom seen with neuromyelitis optica, but it is the *sine qua non* of multiple sclerosis. Hassin<sup>170</sup> explained that the plaques of multiple sclerosis are composed of fibrillary astrocytes, which are rarely seen in the other disease.

7. Size of Lesions: In neuromyelitis optica the lesions may be very large (one lesion may involve several segments of the spinal cord—fourteen continuous segments in Beck's case), whereas the plaques of multiple sclerosis are small and circumscribed.

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170. Hassin, G. B.: *Histopathology of the Peripheral and Central Nervous System*, New York, Paul B. Hoeber, Inc., 1940, pp. 106-117.

171. Lowenberg, K., in discussion on Putnam and Forster,<sup>27</sup> pp. 22-23.

8. Other Pathologic Differences: McAlpine<sup>25</sup> stressed the degree of severity as a differentiating factor, stating that the acute necrosis of neuromyelitis optica is not observed with multiple sclerosis. Other authors have said that the acute process in neuromyelitis optica involves whole bundles of nerve fibers at one time, whereas in multiple sclerosis this wholesale destruction does not occur; instead, single nerve fibers undergo successive degeneration. The proliferation of capillaries seen in neuromyelitis optica was given as a differential point by Balser<sup>18</sup> and McAlpine,<sup>25</sup> who had not seen this proliferation in multiple sclerosis.

*The Diffuse Scleroses.*—In 1912 Schilder<sup>172</sup> described a malady of children and young adults characterized by sudden loss of vision, spastic paralyses, mental deterioration and death in a few months. Pathologically, he observed symmetric diffuse demyelination of the centrum ovale. He called this syndrome "encephalitis periaxialis diffusa," but it has become better known as Schilder's disease. Bouman<sup>173</sup> collected 24 cases of this syndrome in 1924 and published the first survey of the meager literature. She found Schilder's disease characterized histologically by demyelination, destruction of axons, proliferation of astrocytes, gliosis and microglial proliferation. Clinically, the common signs were mental deterioration, spastic paralyses, loss of vision, extraocular muscle palsies, facial palsy and dysarthria. Collier and Greenfield<sup>174</sup> stressed the importance of cerebral blindness in this disease, calling it the chief early sign. Stewart and associates<sup>175</sup> found that central deafness may be the first symptom. In 1924 Globus and Strauss<sup>176</sup> discarded Schilder's restriction of the pathologic alterations to the brain proper when they found lesions throughout the cerebrospinal axis. Brock and associates<sup>177</sup> emphasized the importance of the ocular disturbances; they found loss of vision, field defects, optic neuritis, abnormal pupillary reactions, muscle palsies, nystagmus and

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172. Schilder, P.: Zur Kenntnis der sogenannten diffusen Sklerose: Ueber Encephalitis periaxialis diffusa, Ztschr. f. d. ges. Neurol. u. Psychiat. **10**:1-60, 1912.

173. Bouman, L.: Encephalitis Periaxialis Diffusa, Brain **47**:453-488, 1924.

174. Collier, J., and Greenfield, J. G.: The Encephalitis Periaxialis Diffusa of Schilder: A Clinical and Pathological Study, with an Account of Two Cases, One of Which Was Diagnosed During Life, Brain **47**:489-519, 1924.

175. Stewart, T. G.: Greenfield, J. G., and Blandy, M. A.: Encephalitis Peri-Axialis Diffusa: Report of Three Cases with Pathological Examination, Brain **50**:1-29, 1927.

176. Globus, J. H., and Strauss, I.: Progressive Degenerative Subcortical Encephalopathy: Schilder's Disease, Arch. Neurol. & Psychiat. **20**:1190-1228 (Dec.) 1928.

177. Brock, S.; Carroll, P. M., and Stevenson, L.: Encephalitis Periaxialis Diffusa of Schilder: Report of a Case, Arch. Neurol. & Psychiat. **15**:297-308 (March) 1926.

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170. Hassin, G. B.: *Histopathology of the Peripheral and Central Nervous System*, New York, Paul B. Hoeber, Inc., 1940, pp. 106-117.

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172. Schilder, P.: Zur Kenntnis der sogenannten diffusen Sklerose: Ueber Encephalitis periaxialis diffusa, Ztschr. f. d. ges. Neurol. u. Psychiat. **10**:1-60, 1912.

173. Bouman, L.: Encephalitis Periaxialis Diffusa, Brain **47**:453-488, 1924.

174. Collier, J., and Greenfield, J. G.: The Encephalitis Periaxialis Diffusa of Schilder: A Clinical and Pathological Study, with an Account of Two Cases, One of Which Was Diagnosed During Life, Brain **47**:489-519, 1924.

175. Stewart, T. G.: Greenfield, J. G., and Blandy, M. A.: Encephalitis Peri-Axialis Diffusa: Report of Three Cases with Pathological Examination, Brain **50**:1-29, 1927.

176. Globus, J. H., and Strauss, I.: Progressive Degenerative Subcortical Encephalopathy: Schilder's Disease, Arch. Neurol. & Psychiat. **20**:1190-1228 (Dec.) 1928.

177. Brock, S.; Carroll, P. M., and Stevenson, L.: Encephalitis Periaxialis Diffusa of Schilder: Report of a Case, Arch. Neurol. & Psychiat. **15**:297-308 (March) 1926.



paralyses of gaze. Gasul<sup>178</sup> collected 71 cases from the literature and stated that some loss of vision, with normal pupils, occurred in almost every case.

A number of other demyelinated conditions have been described which differ from Schilder's disease only in name and some minor clinical or pathologic details. Pelizaeus<sup>179</sup> published the clinical features and Merzbacher<sup>180</sup> the pathologic description of what is known as Pelizaeus-Merzbacher disease; this condition also occurs in children and differs from Schilder's disease only in its chronicity and a later onset of blindness. Krabbe<sup>181</sup> reported a variation of diffuse sclerosis in infants, distinctive only in a familial tendency. Scholz<sup>182</sup> described the juvenile form of the cerebral sclerosis, differentiated by a later onset of symptoms (at 8 to 10 years of age). Baló<sup>106</sup> announced the discovery of a new type, characterized by destruction of the cerebral white matter in concentric layers. Indicative of the confusion in this neuro-ophthalmologic jungle is the predicament of Baker and Gerber,<sup>183</sup> who reported a case that was pathologically either of Schilder's or of Krabbe's disease but the patient was too young for Schilder's disease and there was no familial tendency to connect it with Krabbe's type.

*Differential Diagnosis.*—Clinically, many differences have been cited between this group of syndromes and neuromyelitis optica. Most reports have stressed the normal pupil of cerebral blindness (pathognomonic of the diffuse sclerosis) as compared with the dilated, immobile pupil of neuromyelitis optica. The mental deterioration, cortical deafness and other cerebral symptoms of the diffuse sclerosis are not usually found in neuromyelitis optica. The age incidence and the familial tendency in the sclerosis group are also used to differentiate the two conditions. Pathologically, the diffuse sclerosis are

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178. Gasul, B. M.: Schilder's Disease (Encephalitis Periaxialis Diffusa): A Review of the Literature and Report of a Case, *Am. J. Dis. Child.* **39**:595-609 (March) 1930.

179. Pelizaeus, F.: Ueber eine eigenthümliche Form spastischer Lähmung mit Cerebralerscheinungen auf hereditärer Grundlage (multiple Sklerose), *Arch. f. Psychiat.* **16**:698-710, 1885.

180. Merzbacher, L.: Eine eigenartige familiär-hereditäre Erkrankungsform: Aplasia axialis extracorticalis congenita, *Ztschr. f. d. ges. Neurol. u. Psychiat.* **3**:1-138, 1910.

181. Krabbe, K.: A New Familial, Infantile Form of Diffuse Brain-Sclerosis, *Brain* **39**:74-114, 1916.

182. Scholz, W.: Klinische, pathologische-anatomische und erbbiologische Untersuchungen bei familiärer, diffuser Hirnsklerose im Kindesalter: Ein Beitrag zur Lehre von den Heredodegenerationen, *Ztschr. f. d. ges. Neurol. u. Psychiat.* **99**:651-682, 1925.

183. Baker, A. B., and Gerber, L. S.: Cerebral Sclerosis, *Am. J. Dis. Child.* **59**:522-534 (March) 1940.

apparently identical with neuromyelitis optica in microscopic section. The only significant difference lies in the distribution of the lesions, the pathologic changes in the scleroses being mainly cerebral while the lesions of neuromyelitis optica are infrequently observed in the brain.

*The Acute Disseminated Encephalomyelitides.*—Postvaccinal encephalomyelitis has been known ever since jennerian prophylaxis became popular; but, for some unknown reason, a definite increase in the incidence has been noted in the past twenty-five years. Most cases occur, obviously in children, and about one-half the cases are fatal. Cerebral symptoms are prominent, and flaccid paralyses with incontinence are the principal signs of involvement of the spinal cord. The ocular complications were summarized by Herrenschwand<sup>184</sup>; he described (1) optic neuritis with transient blindness, followed by secondary optic nerve atrophy; (2) mild primary optic nerve atrophy; (3) transient paralyses of the oculomotor nerve, and (4) bilateral palsies of the abducens nerve. The pathologic features (Turnbull and McIntosh<sup>185</sup>) consist of congestion of the brain and spinal cord, destruction of the gray matter, perivascular demyelination and lymphocytic infiltration. Perdrau<sup>186</sup> found the lesions similar to those of multiple sclerosis. An encephalomyelitis also follows smallpox (Wilson and Ford,<sup>187</sup> Marsden and Hurst<sup>188</sup>) that is indistinguishable from that following vaccination. Encephalitis following Pasteur prophylaxis against rabies has not infrequently been reported; the lesions are histologically similar to those of the other encephalomyelitides. Ocular lesions are not prominent.

Postmeasles encephalomyelitis has been known for one hundred years; it occurs in about 0.5 per cent of cases of measles, coming on about five days after the onset of the exanthem. A wide variety of symptoms are encountered, according to the location of the lesions. A number of pathologic patterns have been described by Ford<sup>189</sup>: a meningismus-like type, multiple focal lesions, single focal lesions, a cerebellar type, a spinal cord type and optic neuritis alone. This

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184. Herrenschwand, F.: Zur Beteiligung des Sehnerven bei Encephalomyelitis Postvaccination, *Klin. Monatsbl. f. Augenh.* **102**:815-823, 1939.

185. Turnbull, H. M., and McIntosh, J.: Encephalomyelitis Following Vaccination, *Brit. J. Exper. Path.* **7**:191-222, 1926.

186. Perdrau, J. R.: The Histology of Post-Vaccinal Encephalitis, *J. Path. & Bact.* **31**:17-32, 1928.

187. Wilson, R. E., and Ford, F. R.: Nervous Complications of Variola, Vaccinia, and Varicella, *Bull. Johns Hopkins Hosp.* **40**:337-353, 1927.

188. Marsden, J. P., and Hurst, E. W.: Acute Perivascular Myelinoclasia ("Acute Disseminated Encephalomyelitis") in Smallpox, *Brain* **55**:181-225, 1932.

189. Ford, F. R.: The Nervous Complications of Measles, with a Summary of the Literature and Publication of Twelve Additional Case Reports, *Bull. Johns Hopkins Hosp.* **43**:140-184, 1928.

variability explains the diverse ocular findings, i. e., papilledema, optic neuritis, dilated pupils, central scotomas, homonymous hemianopsias, visual hallucinations and extraocular muscle palsies. Measles encephalitis sometimes closely resembles neuromyelitis optica. Encephalomyelitis following rubella has also been described (Margolis, Wilson and Top<sup>190</sup>); diplopia, nystagmus and sluggish pupillary reactions constitute the reported ocular findings.

A more benign form of encephalomyelitis is seen after chickenpox (Walsh<sup>58</sup>), similar in every way to the postmeasles type except in severity. Ophthalmologically, optic neuritis, with visual loss, optic nerve atrophy, ptosis, extraocular muscle palsies and nystagmus, has been reported. There is a high rate of recovery (about 90 per cent), both from the general and from the ophthalmologic point of view. Ferraro<sup>191</sup> reported a similar encephalomyelitis following scarlet fever. A severe encephalomyelitis occurs in conjunction with mumps; this type is usually associated with meningitis and is not likely to be confused with the demyelinating diseases. Scheinker,<sup>192</sup> however, reported a case of mumps encephalomyelitis similar in all respects to the postmeasles and postvaccination types.

*Differential Diagnosis.*—Clinically, there is little in common between these encephalomyelitides and neuromyelitis optica. The history of the preceding infection or vaccination usually points to the diagnosis in the former conditions, which occur in great preponderance in children. The prominence of the cerebral signs and symptoms and the frequent involvement of the cerebellum in the disseminated encephalomyelitides constitute important clinical differences. The only similarity of any consequence is the involvement of the optic pathway that is common to both neuromyelitis optica and the encephalomyelitides. Pathologically, the latter conditions differ from neuromyelitis optica in that (1) they exhibit small, discrete lesions that do not tend to coalesce into large foci, (2) they commonly show gliosis and (3) their lesions reveal a decided inflammatory nature.

*Comment.*—It is obvious that the demyelinating diseases exhibit many similarities, and especially is this true of multiple sclerosis and neuromyelitis optica. It must be admitted that in some cases Devic's disease is indistinguishable clinically from multiple sclerosis. Many

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190. Margolis, F. J.; Wilson, J. L., and Top, F. H.: Post-Rubella Encephalomyelitis: Report of Cases in Detroit and Review of Literature, *J. Pediat.* **23**:158-165, 1943.

191. Ferraro, A.: Allergic Brain Changes in Post-Scarlatinal Encephalitis, *J. Neuropath. & Exper. Neurol.* **3**:239-254, 1944.

192. Scheinker, I. M.: Disseminated Encephalomyelitis and Its Relation to Multiple Sclerosis, *J. Neuropath. & Exper. Neurol.* **2**:418-419, 1943.

of the differences in the clinical picture (differences in course, visual loss and presence or absence of cerebral symptoms) can be plausibly explained as the result of variation in the severity of the process, in the location of lesions and in the reaction of the patient. Other differences are difficult to explain. The fact that nystagmus is seen in almost all cases of advanced multiple sclerosis, and yet is rare in neuromyelitis optica, is one such problem. The common occurrence of optic neuromyelitis in children, whereas multiple sclerosis is not seen before puberty, is another factor not easily elucidated.

In the same manner, most of the variations in the pathology may well be due to differences in the location and severity of lesions. The involvement of the gray matter, the destruction of axis-cylinders, the more abundant cellular exudate and the greater size of the lesions in neuromyelitis optica, as compared with multiple sclerosis, might be attributed to the factors mentioned. Again, however, there are dissimilarities that are not easily explained. One of these is the occurrence of cavitation in neuromyelitis optica and the lack of it in multiple sclerosis, even in the so-called acute multiple sclerosis. Another is the universal occurrence of gliosis (plaques) in multiple sclerosis and the paucity of gliosis (and total lack of plaques) in neuromyelitis optica, even in the more chronic cases.

One must remember that neuromyelitis optica is usually seen at autopsy in the early, acute stage, while multiple sclerosis is seldom seen except in a late stage of the chronic type in old patients who die of some other cause. This suggests an interesting objective point of differentiation, namely, that patients die of neuromyelitis optica but not of multiple sclerosis. This factor offers ground for interesting speculation. So much has been written about the pathology of multiple sclerosis, and yet there is a dearth of material classified under that diagnosis in our pathologic laboratories. In the pathologic collection of the Presbyterian Hospital (representing over 15,000 autopsies, performed in the past thirty years), there are no cases in which death was due to multiple sclerosis. (There are 3 cases listed under that diagnosis, but in each instance the diagnosis was secondary, the patient having old multiple sclerosis but dying of some other cause). The rarity of pathologic material is not mentioned in the voluminous literature on multiple sclerosis, and yet many writers discuss the pathology of active multiple sclerosis with assurance. These facts tend to weaken some of the positive statements frequently made regarding the similarity of the pathology of this disease to that of neuromyelitis optica.

Moreover, if one accedes pathologic similarity in these diseases, the problem is still not solved. The crux of the matter then becomes whether or not clinical and histologic similarity is sufficient basis for hypothesizing a common etiology, and so identity. It must be admitted

that it is not. Clinical likenesses are notoriously fallible for purposes of such an assumption. Pathology as the basis for etiologic diagnosis has already been discussed under etiology. To repeat, there appears to be no logical reason for assuming a common cause because of similar, or even identical, pathology.

With regard to the diffuse scleroses, there is no substantial reason for so many different forms, the differentiation relying on such insecure factors as age at onset, duration of course and questionable familial tendencies. Their main bond with neuromyelitis optica is the similarity of the histologic picture, and, for the reasons already given, this does not prove a common identity. The same comment pertains to the acute encephalomyelitides. In fact, the initiation of this pathologic picture by so many different stimuli in the encephalomyelitides might well be offered as an argument against the unity of the demyelinating diseases.

#### SUMMARY

In view of the new theory of the common identity of the demyelinating diseases, neuromyelitis optica assumes a new importance. It has a much greater mortality rate than multiple sclerosis and therefore affords more material for pathologic study.

The important early contributions to the study of neuromyelitis optica are summarized, and the literature since 1927 is briefly discussed.

Five cases of neuromyelitis optica have been diagnosed in the Columbia-Presbyterian Medical Center in the past twenty years. The clinical records and the pathologic findings of these cases are presented.

Twenty cases of neuromyelitis optica, substantiated by postmortem examination, were studied in an effort to establish the common clinical features. This survey showed that this disease occurs commonly between the ages of 30 and 50 years, more often in females and is not limited to persons of the white race. The initial symptoms are referable to the visual system in one-half the cases and to the spinal cord in the rest. Severe binocular loss of vision is characteristic. In most cases there was optic nerve atrophy of some kind, associated with a central scotoma or complete loss of the visual field. The rapidly ascending nature of the myelitis is the only characteristic neurologic finding. Remissions occur in about one-half the cases. The patient frequently dies in the first three months of his illness, and in the fatal cases the survival is seldom over two years. There are no characteristic laboratory findings and no efficacious therapy.

The pathologic features in these 20 cases were also surveyed. It was found that the lesions of neuromyelitis optica commonly occur in the optic pathway, spinal cord and brain stem, and occasionally in the cerebrum. Histologically, the disease is characterized by demyelination

of nerves, destruction of axis-cylinders, mild astrocytosis, pronounced microglial proliferation, perivascular infiltration of white blood cells, proliferation of capillaries and, sometimes, gross cavitation.

A composite, chronologic description of the microscopic process in neuromyelitis optica, with illustrative photomicrographs, is presented.

The five principal etiologic theories of the demyelinating diseases are (1) the infectious theory, (2) the toxic theory, (3) the enzyme theory, (4) the theory of vascular obstruction and (5) the allergic theory. None of these theories has been substantiated. The evidence for and against each is weighed.

It is suggested that too much emphasis has been placed on the most obvious finding in these diseases, namely, demyelination of nerve fibers. Demyelination appears to be one of the first reactions of nerve tissue to trauma, and a multitude of injuries may cause this loss of myelin. There is no evidence, therefore, that demyelination is of any particular etiologic or pathologic significance.

The hypothesis of the common etiology of the demyelinating disease group rests mainly on the demonstration of a similar pathologic process. It is suggested, however, that the demonstration of similar, or even identical, pathologic changes does not prove the existence of a common etiologic agent. It would appear more logical to attempt to fulfil Koch's postulates in the conventional manner.

The case reports in this paper are presented with the permission of Dr. Edwin G. Zabriskie, acting director of the Neurological Institute of New York.

The pathologic material was made available to me by Dr. Harry Pratt Smith, director of pathology, Presbyterian Hospital.

Dr. Abner Wolf and Dr. David Cowen rendered invaluable assistance in the interpretation of the pathologic picture.

Dr. Frank P. Carroll assisted in the interpretation of the ophthalmologic findings.

704 State Tower Building.

## News and Notes

EDITED BY DR. W. L. BENEDICT

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### GENERAL NEWS

**National Society for the Prevention of Blindness.**—The National Society for the Prevention of Blindness will hold a five day conference in conjunction with the interim session of the Pan-American Association of Ophthalmology, March 26 to 30, 1950, at the Floridian Hotel, Miami Beach, Fla. The theme of the meeting will be "The Americas Unite to Save Sight"; and among the subjects to be discussed are current blindness prevention programs in countries of the Western Hemisphere, trachoma, industrial ophthalmology, ophthalmologic problems of school children and medical and social management of the glaucomas.

Persons directly or indirectly concerned with the health and safety of the eyes will find this conference of interest. Details concerning the program may be obtained by writing directly to the National Society for the Prevention of Blindness, 1790 Broadway, New York 19.

Reservations should be made in the near future with the Floridian Hotel, 540 West Avenue, Miami Beach, Fla.

**Annual Spring Graduate Course of the Gill Memorial Eye, Ear and Throat Hospital.**—The Twenty-Third Annual Spring Graduate Course of the Gill Memorial Eye, Ear and Throat Hospital will be held in Roanoke, Va., April 3 to 8, 1950. The guest faculty is as follows:

Dr. F. W. Stocker, Durham, N. C.; Dr. Conrad Berens, New York; Dr. Fred Wilson, Chicago; Dr. C. W. Mayo, Rochester, Minn.; Dr. Edmund B. Spaeth, Philadelphia; Dr. Arthur J. Bedell, Albany, N. Y.; Dr. James J. Regan, Boston; Dr. W. Gayle Crutchfield, Charlottesville, Va.; Dr. Stuart Cullen, Iowa City; Dr. Richard G. Scobee, St. Louis; Dr. Daniel S. Cuning, New York; Dr. Alson E. Braley, New York; Dr. Karl M. Houser, Philadelphia; Dr. Hugo L. Bair, Rochester, Minn.; Dr. Gabriel Tucker, Philadelphia; Dr. Edward M. Walzl, Baltimore; Sir Alexander Fleming, London, England; Dr. J. Barrett Brown, St. Louis; Dr. Walter B. Hoover, Boston; Dr. Oscar C. Hansen-Pruss, Durham, N. C.

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### CORRECTION

In the article by Dr. K. W. Ascher entitled "Aqueous Veins and Their Significance for Pathogenesis of Glaucoma," published in the July issue of the ARCHIVES, line 9 on page 67 should read, "eye" and in eyes of experimental animals<sup>8</sup>; they can be photographed . . ."

# Abstracts from Current Literature

EDITED BY DR. WILLIAM ZENTMAYER

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## Cornea and Sclera

SJÖGREN SYNDROME. C. ESPILDORA LUQUE, J. MOSSER and A. GORMAZ, Arch. Soc. oftal. hispano-am. 8: 333 (April) 1948.

The filamentous keratitis associated with diminished lacrimal secretion, mentioned by Wagenmann and Leber at the end of the last century, was the first symptom of the Sjögren syndrome to be described. In 1919 Fuchs related his observation of a case and suggested the possibility of the association of this symptom with a systemic condition. This was a further step in the description of the syndrome in question. After this many authorities reported similar cases, until Sjögren made a full study of the condition and described all the symptoms which constitute the syndrome now bearing his name.

The authors are of the opinion that the filamentous keratitis primarily described by Wagenmann and Leber is not of a type associated with this syndrome. The type occurring in this pathologic entity is microscopic. The filaments present are in the form of fine, white threads, lying loose on the cornea and floating in a grumous, sticky fluid, which forms a whitish foam at both canthi.

The keratoconjunctivitis sicca described by Duke-Elder is the one which integrates the Sjögren syndrome, being accompanied with dryness of the conjunctiva and of the mucous membrane of the mouth, pharynx and larynx, hypertrophy of the parotid gland, arthritis, and other changes.

The syndrome may or may not be initiated by the ocular symptom. In 9 cases reported by the authors the ocular manifestations began many years after onset of the arthritis. In other cases the condition was initiated by an acute inflammation of the salivary glands or by dryness of the mouth.

A detailed discussion of the etiology, pathogenesis, symptomatology, differential diagnosis and treatment of the syndrome is made. Nine new cases are reported.

The article is illustrated.

H. F. CARRASQUILLO.

SUBCONJUNCTIVAL INJECTIONS OF BLOOD IN MANAGEMENT OF DISEASES OF THE CORNEA. Z. PALTZEVA, Vestnik oftal. 25: 34, 1946.

Paltzeva used diluted blood in the treatment of 33 patients with purulent corneal ulcers and of 5 patients with herpetic keratitis. The technic was as follows: To 0.45 cc. of distilled water in the syringe is added 3 drops of blood taken from the patient's finger; the mixture is shaken until it becomes transparent, and 0.2 of it is injected subconjunctivally near the limbus.

The injections were given every other day for a total of two to eight injections. Trauma was the etiologic factor in the corneal ulcer in



20 cases. Bacteriologic examination showed the presence of the white staphylococcus in 14 cases, the pneumococcus in 7 cases and the streptococcus in 3 cases. In 20 cases epithelization of the ulcer occurred after two to four injections, and in the others from five to eight injections were required for complete epithelization of the cornea and absorption of the hypopyon. The blood count showed an increase of the red and the white blood cells.

Paltzeva believes that it is worth while to try this simple method, as no complications were observed, the subjective symptoms were relieved and epithelization and absorption of hypopyon were speeded up. Case histories and a table illustrate the improvement of vision.

O. SITCHEVSKA.

### **Glaucoma**

PROVOCATIVE TESTS IN THE DIAGNOSIS OF THE GLAUCOMAS. H. S. SUGAR, *Am. J. Ophth.* 31: 1193 (Oct.) 1948.

Sugar concludes that the combined water and pressor-congestion test gives higher responses in cases of glaucoma than either of these tests alone. In the combined test a rise of over 10 mm., or to over 38 mm., may be considered positive. No provocative test is of greater diagnostic value than routine and repeated tonometry in diagnosis of glaucoma in patients over 40 years of age.

W. S. REESE.

GONIOSCOPIC FINDINGS IN PRIMARY GLAUCOMA. J. FRANCOIS, *Ann. d'ocul.* 181: 399 (July) 1948.

The author discusses the various changes in the angle of the anterior chamber that are said to occur in glaucoma. Barkan's classification of wide and narrow angle glaucoma is referred to. The data on 32 cases of glaucoma are presented. From these, the author concludes that in chronic simple glaucoma there are no pathognomonic signs in the angle. One may find certain abnormalities, but they are also seen in eyes that do not have increased tension. In congestive glaucoma the angle is very narrow when the tension is raised. After the congestive phase numerous synechias are found; these are more numerous if the tension has been raised for some time. In unilateral chronic simple glaucoma the angles of the eyes appear the same. In congestive glaucoma the angle is always narrower in the diseased eye.

P. R. McDONALD.

BASAL METABOLISM IN GLAUCOMA. A. KOLENKO, *Vestnik oftal.* 25: 45, 1946.

The basal metabolism was measured in 100 patients with glaucoma; of these 71 patient had primary glaucoma, in various stages, and 29 had secondary glaucoma. Lowering of the basal metabolic rate was observed in some patients with primary glaucoma. There was no increase of the basal metabolism in the patients with secondary glaucoma. Further investigation will follow.

O. SITCHEVSKA.

### Experimental Pathology

EXPERIMENTAL DIABETIC CATARACT IN RATS. F. E. D. CRAMER and V. G. FOGLIA, *Arch. de oftal. de Buenos Aires* 13:101 (April-June) 1948.

Experiments were conducted on depancreatized rats to observe the development of cataract. The removal of 95 per cent of the pancreas by the technic of one of the authors (Foglia) produced diabetes within six months in 92 per cent of the male rats and in 28 per cent of the female rats. The rats lived seven months or more, allowing plenty of time for study of the formation of lenticular opacities. The diabetic cataract appeared in these rats at least seventy days after 95 per cent of the pancreas was removed and two hundred days after only 80 per cent of the organ was excised. Once the first changes made their appearance, the alterations continued until the lens became totally opaque.

The progress in the development of the opacities was in relation to the intensity of the diabetes present in the animal. In no case did retrograde changes take place after the cataract was formed. The lens showed pronounced histologic changes, as well as chemical modifications. The article is illustrated.

H. F. CARRASQUILLO.

### General Diseases

TUBERCULOSIS OF THE CHOROID IN A CASE OF MILIARY TUBERCULOSIS TREATED WITH STREPTOMYCIN. J. P. HALBERG, *Ann. d'ocul.* 181:485 (Aug.) 1948.

The authors report the case of a 16 year old boy with miliary tuberculosis who showed evidence of miliary tubercles in the choroid of both eyes. He received 247.5 Gm. of streptomycin over a period of four months, with no toxic manifestations. The pulmonary tuberculosis receded rapidly, and the choroidal lesions showed progressive cicatrization.

P. R. McDONALD.

TOXOPLASMOSIS. C. D. BINKHORST, *Ophthalmologica* 115:65 (Feb.) 1948.

The clinical signs most commonly encountered in cases of toxoplasmosis in infants are chorioretinitis, cerebral calcifications, encephalomyelitis with hydrocephalus, fits, vomiting, fever, paresis, xanthochromia and an increase of albumin and cells in the spinal fluid. In adults the most frequent findings are pneumonia, fever, exanthems and gastroenteritis. In most cases the chorioretinitis is circumscribed, bilateral and central. The condition is frequently acquired in utero and is then usually fatal. Diagnosis is based on biopsy observations, the complement fixation reaction, changes in the spinal fluid and the appearance of toxoplasmas in the mouse brain after intracerebral injection of infected spinal fluid.

This report is the first in the European literature of a case in which the diagnosis was made during life by the demonstration of toxoplasma-like parasites in the mouse brain after the injection of spinal fluid. The article is illustrated.

H. P. KIRBER.

CHANGES IN THE EYE, ESPECIALLY IN THE FUNDUS, ACCOMPANYING TUBERCULOSIS OF THE SKIN. L. NÉMETH, *Ophthalmologica* 115: 167 (March) 1948.

The author includes under the heading "tuberculoderma" lupus, scrofuloderma, lupus erythematosus, erythema induratum (Bazin's disease) and sarcoidosis (Boeck's sarcoid). Of 36 cases of tuberculoderma he found changes in the eyegrounds in 8. In 6 of these cases an old choroiditis existed, and in 2, papillitis, retinitis and small tubercles. The acute exudative, as well as the chronic proliferative, type of tuberculosis involving the choroid, retina and optic nerve can be found in patients with tuberculosis of the skin. H. P. KIRBER.

### Lids

SOME METHODS OF LID REPAIR AND RECONSTRUCTION. S. A. FOX, *Am. J. Ophth.* 31: 1441 (Nov.) 1948.

Fox describes an operative method of constructing an inferior cul-de-sac which is essentially the old method of Snellen sutures.

W. S. REESE.

TREATMENT OF HORDEOLUM WITH INTRAPALPEBRAL INJECTION OF PENICILLIN. M. T. ROSAS COSTA, *An. Argent. de oftal.* 8: 13 (Jan.-March) 1947.

The author believes that the use of penicillin is the most efficacious of all methods of treatment of hordeolum. He uses it locally in perifocal injection. He injects 50,000 Oxford units dissolved in 1 cc. of a 2 per cent solution of procaine hydrochloride. The hordeolum is cured in from twelve to twenty-four hours. H. F. CARRASQUILLO.

### Neurology

INVOLVEMENT OF THE OPTIC CHIASM IN VON RECKLINGHAUSEN'S DISEASE (NEUROFIBROMATOSIS). P. E. TIKHOMIROV, *Vestnik oftal.* 26: 25, 1947.

Involvement of the visual apparatus in neurofibromatosis occurs in the lids in the form of plexiform neurofibroma, or fibroma molluscum; in the conjunctiva, sclera, cornea, iris, choroid and ciliary body, nodules are observed occasionally. Tumors in the retina, the optic nerve and the optic chiasm may also be present. Hydrophthalmos, glaucoma, optic nerve atrophy, defects of the orbital walls and enlargement of the sella turcica may be secondary to general neurofibromatosis.

Tikhomirov reports a case of neurofibromatosis with the rare occurrence of tumor in the chiasm. A woman aged 35 was hospitalized because of blindness in the left eye and impairment of vision in the right eye. There was a mature cataract in the left eye with faulty light projection. In the left eye, vision was reduced to 0.5, and there were atrophy of the optic nerve and concentric constriction of the visual fields. The roentgenogram showed destruction of the sella turcica and

the upper medial wall of the optic canal with its enlargement. The patient had multiple pigmented neurofibromas on the neck, the back and the extremities.

Thus, the descending optic nerve atrophy of both eyes and the destruction of the posterior wall of the sella turcica indicated the presence of an intrasellar tumor, which, in view of the general neurofibromatosis, could be classified as of the neurinoma or the schwannoma type.

O. SITCHEVSKA.

### Ocular Muscles

ANALYSIS OF OCULAR MOTOR ANOMALIES. W. C. OWENS, *Am. J. Ophth.* 31:1297 (Oct.) 1948.

Owens describes the motility clinic at Johns Hopkins Hospital and emphasizes the necessity of a standardized method of analysis of oculomotor anomalies.

W. S. REESE.

FACTORS IN THE SURGICAL TREATMENT OF VERTICAL DEVIATIONS. J. H. DUNNINGTON, *Am. J. Ophth.* 31:1404 (Nov.) 1948.

Dunnington points out that recent knowledge has shown that most deviations of vertically acting muscles are of paralytic origin. Selection of the proper operative procedure in a given case of paralysis depends not only on the amount of deviation present in the various directions of gaze but also on the eye used for fixation. The surgical treatment of each type of paralysis is reviewed, and the importance of the "fixing eye" in the selection of the proper surgical approach is pointed out.

W. S. REESE.

POSTOPERATIVE HYPERTROPIA. R. G. SCOBEE, *Am. J. Ophth.* 31:1437 (Nov.) 1948.

In this interesting article, Scobee states that there is no such thing as unintentional postoperative hypertropia. It is really preoperative and simply requires careful diagnostic study for its recognition.

W. S. REESE.

### Operations

TECHNIC OF FINISHING THE KERATOTOMY AND MAINTAINING THE SPHINCTER OF THE IRIS WHEN THE KNIFE ENGAGES THE IRIS. J. SÉDAN and S. SÉDAN-BAUBY, *Ann. d'ocul.* 181:414 (July) 1948.

The authors state that in cataract extractions a keratome incision enlarged with scissors is popular on the Continent and in the United States. There are many surgeons, however, who prefer to use a Graefe knife. One of the disadvantages of using a Graefe knife is that the iris may be caught on the knife, and if the corneal section is completed a ragged iridectomy is obtained. The authors believe that preservation of the sphincter of the iris is important and that every possible means should be taken to preserve its integrity. The literature on the avoidance and handling of this complication is reviewed.

The authors present their methods of handling this complication. Their method of choice is to withdraw the Graefe knife if the iris is caught and to reinsert a knife with a dull rounded tip. The tip of the knife is carried across the anterior chamber in the region of the angle until the point of counterpuncture is reached. The section is then completed in the regular manner. In a number of cases they have completed the section, using Castroviejo's corneal scissors. They prefer the use of a dull-tipped knife, since its use permits the sectioning of a conjunctival flap.

P. R. McDONALD.

### Physiology

VISUAL PURPLE AND THE PHOTOPIC LUMINOSITY CURVE. H. J. A. DARTNALL, Brit. J. Ophth. 32:793 (Nov.) 1948.

The present article is concerned with the quantitative consideration of the present hypothesis that visual purple mediates the luminosity sensations of both scotopic and photopic vision and offers a *prima facie* explanation of the reduced sensitivity of photopic vision and of the Purkinje shift associated with light adaptation. Two main assumptions are made in developing the hypothesis. The first of these is that the production of visual purple from its precursors is a rapid process as compared with regeneration from its photoproducts; the second, that the influence of absorption by the photoproducts on the light absorbed by visual purple is equal to that obtaining in a homogenous mixture of the substances. It is shown that the effect of the accumulation of photoproducts (indicator yellow) in a retina exposed to light is to move the position of maximum light absorption by visual purple toward the longer wavelengths. This process is not indefinitely prolonged. As the amount of indicator yellow accumulates the light absorbed curve of visual purple rapidly approximates to a limiting position having a maximum at about 550 millimicrons. When this limiting curve is corrected for absorption by the ocular media and by the macular pigment, the resulting curve closely approximates the photopic luminosity curve. In addition to accounting for the Purkinje shift in a quantitative manner, the hypothesis provides a basis for the explanation of a number of other visual phenomena, notably the reduced sensitivity of photopic vision and the dependence of the rate of dark adaptation on the previous light history of the retina.

W. ZENTMAYER.

### Refraction and Accommodation

THE FOGGING METHOD OF REFRACTION. J. M. O'BRIEN and R. E. BANNON, Am. J. Ophth. 31:1453 (Nov.) 1948.

O'Brien and Bannon find from refraction of 500 patients that there is agreement in a large percentage of cases between the cycloplegic and the fogging method of refraction. They feel that the capable refractionist should be familiar with the technic of fogging and the limitations of its use, as its efficacy and ease make it a valuable office procedure.

W. S. REESE.

BINOCULAR REFRACTION. P. W. MILES, *Am. J. Ophth.* 31:1460 (Nov.) 1948.

Miles considers binocular refraction a valuable refinement which permits more exact balance in the sphere between the two eyes and more exact determination of the astigmatic axis in the position of action. Binocular refraction is not useful in the absence of fusion and is less efficient when one eye is inferior to the other.

W. S. REESE.

DATA CONCERNING THE HEREDITY OF ASTIGMATISM. I. BIRO, *Ophthalmologica* 115:156 (March) 1948.

The author examined 31 members of three generations of one family and found astigmatism to be of irregular dominance. He concludes that not only hypermetropia, myopia and astigmatism are hereditary, a fact which has long been known, but that their degree and axis are also inherited.

H. P. KIRBER.

### Retina and Optic Nerve

A STUDY OF THE ANGLE OF BIFURCATION OF RETINAL VESSELS. C. W. WASMUND, *Am. J. Ophth.* 31:12 (Jan.) 1948.

Wasmund used Bedell's fundus photographs in a study of the angle of bifurcation of normal and arteriosclerotic retinal arteries. He found the average angle 70 degrees in normal and 82 degrees in arteriosclerotic fundi, this finding being contrary to the generally accepted statements in the literature.

W. S. REESE.

BLOOD SUPPLY OF THE OPTIC NERVE AND ITS CLINICAL SIGNIFICANCE. D. VAIL, *Am. J. Ophth.* 31:1 (Jan.) 1948.

Vail reviews the gross anatomy of the optic nerve and chiasm, the relations of the nerve, the circulation of the spinal fluid and blood supply. He discusses these aspects from the standpoint of their clinical significance.

W. S. REESE.

FATTY EMBOLISM OF THE RETINAL ARTERY FOUND IN EYES AFTER ENUCLEATION AND ORBITAL EXENTERATION. A. LOEWENSTEIN and J. FOSTER, *Brit. J. Ophth.* 32:819 (Nov.) 1948.

While studying the retina with the slit lamp after equatorial opening of the excised eye, the authors observed, on 4 occasions, that the central artery was partly filled with fat. In the first case excision was for a malignant melanoma of the choroid in the macular area; in the second, for a malignant melanoma of the limbus, and in the third, for a perforating injury of the eyeball; in the fourth an exenteration of the orbit had been done for malignant melanoma. The embolus was more or less fluid and consisted of a fine fatty emulsion, which stained shining red with scarlet red. The fatty content of the central artery is assumed to have been aspirated from the orbital fat and emulsified by the blood. Fatty embolism of the central artery with white silvery retinal patches and superficial hemorrhages is relatively frequent with fractures of the long bones and is probably the cause of Purtscher's traumatic retinal

angiopathy. The proved fine emulsion of the fat in these 4 cases may explain the as yet inexplicable passage of fat through the pulmonary capillaries.

W. ZENTMAYER.

INTERSTITIAL OPTIC NEURITIS FOLLOWING A FURUNCLE OF THE NASAL VESTIBULE. I. TETZU, N. BLATT and J. SILVIAN, Arch. d'opht. 8: 264, 1948.

The authors describe a case of a man aged 55 in whom an optic atrophy developed after a furuncle of the nose. This man was treated with large doses of sulfonamide drugs and penicillin. They discuss the etiologic development of the complications which may arise from infections about the nose involving the eye and orbit. The literature is reviewed. They point out that not only many orbital and cavernous sinus complications arise but that severe iridocyclitis and thrombosis of the central retinal vein and panophthalmitis can also occur. They believe that if the patient is undergoing antisyphilitic treatment this treatment should be stopped until the acute phase has subsided, since arsenic, bismuth and mercury are especially harmful to the optic nerve. Although a number of authors are cited, no bibliography is submitted.

S. B. MARLOW.

### Therapeutics

AUREOMYCIN IN OCULAR INFECTIONS. A. E. BRALEY and M. SANDERS, J. A. M. A. 138: 426 (Oct. 9) 1948.

Aureomycin borate in 0.5 to 1 per cent solution is nonirritating to the inflamed conjunctiva and only slightly irritating to the noninflamed conjunctiva. Aureomycin borate is effective in 0.5 per cent concentration in the treatment of staphylococci and pneumococcic infections, influenza and inclusion blennorrhea. The antibiotic appears to be effective in cases of rodent (Mooren's) ulcer and of atypical rodent ulcer of unknown cause. Aureomycin has some effect in epidemic keratoconjunctivitis, provided treatment is started before the fourth day of the disease. Aureomycin may be of value in dendritic keratitis. Aureomycin is a valuable addition to the armamentarium of antibiotics.

J. A. M. A. (W. ZENTMAYER.)

### Trachoma

ON GENESIS AND OPERATION OF THE CICATRICIAL (TRACHOMATOUS) ENTROPION OF THE UPPER LID. A. KETTESY, Brit. J. Ophth. 32: 419 (July) 1948.

Kettesy describes the genesis of entropion of the upper lid, the result of trachoma, and the operation he has devised to correct the deformity of the lid. The upper lid is everted by Liebermann sutures. The tarsus is divided completely in its thickness and length by an incision in the scar line of the sulcus subtarsalis. Three mattress sutures are inserted into the conjunctival margin of the section, taking up some tarsal tissue. To facilitate the turning out of the marginal tarsal strip, an incision is made the full length of the strip without buttonholing the skin. The mattress sutures are brought out through the marginal tarsal strip. After loosely knitting the sutures, the diverg-

ing ends are brought horizontally through the skin of the lid 10 to 12 mm. higher and knotted. This prevents tilting of the new intermarginal surface and secures an overcorrection.

The article is illustrated to show the steps of the operation.

W. ZENTMAYER.

### Tumors

A CASE OF PIGMENTED LEIOMYOMA OF THE IRIS. N. FLEMING, Brit. J. Ophth. 32: 885 (Dec.) 1948.

Fleming reports a case of a tumor involving apparently the whole breadth of the iris and extending over the lower and inner third of its circumference. The growth was removed by iridectomy. The pathologic diagnosis was leiomyoma of the iris with included pigment granules. The tumor had a uniform structure throughout. It was composed of spindle cells with spindle nuclei and moderately long cytoplasmic bodies. The arrangement of the cells was that commonly seen in neurofibromas, with much pigment throughout the tumor. Some of the pigment is present in a few of the cells, so that it may seem justifiable to regard the tumor as a melanotic neuroectodermal leiomyoma. In considering similar cases in the literature, Fleming states the belief that this group should not be classified offhand as leiomyoma of neuroectodermal muscle but that the point should be kept open as to whether such growths do not present characteristics that make this classification as leiomyoma as anomalous as that of the neuroectodermal musculature from which they appear to be derived.

W. ZENTMAYER.

### Uvea

USE OF IMMUNE GLOBULIN IN THE TREATMENT OF UVEITIS. B. KRONENBERG, Am. J. Ophth. 31: 1271 (Oct.) 1948.

Kronenberg gives a preliminary report of the use of immune globulin in treatment of acute forms of uveitis. In a number of cases it appeared to help in clearing up a severe uveitis which did not respond to the usual therapy.

W. S. REESE.

UVEOPIGMENTARY SENSITIZATION. H. H. JOY, Am. J. Ophth. 31: 1581 (Dec.) 1948.

Joy discusses sympathetic ophthalmia, as well as the Vogt-Koyanagi syndrome and Harada's disease, from the standpoint of allergic response to uveal pigment. He feels that further proof must be presented to prove that the latter conditions are due to uveal pigment allergy.

W. S. REESE.

ATROPHIA GYRATA CHOROIDEAE ET RETINAE. J. SAEB, Brit. J. Ophth. 32: 824 (Nov.) 1948.

The disease was demonstrated in 4 brothers but in neither their ascendants nor their descendants. There was a uniform clinical picture, the variations being attributable to the progress of the disease. It is reasonable to believe that the development of the condition would result in total atrophy of the choroid and retina, producing a picture resembling that of choroideremia. Nothing has been found to justify the continued classification of atrophía gyrata and choroideremia as



two distinct conditions, doing away with the concept that the former is an acquired, progressive degeneration (atrophy) and the latter a chorioretinal defect or malformation. Colored plates well illustrate the condition in the 4 cases.

W. ZENTMAYER.

CHRONIC IRIDOCYCLITIS. A. LUND, *Acta ophth.* 22: 176, 1944.

The treatment for chronic iridocyclitis given in the Finsen Institute is based on the assumption that the lesion is tuberculous and consists principally in a protracted series of carbon arc light baths together with injections of human tubercle bacillus protein. The author reviews a series of 88 patients, 30 male and 58 female, representing 151 affected eyes. These patients were followed closely for several years. In most patients the lesion made its appearance at the age of 20 to 30. The morbidity rate for women was also increased at about the age of 50. The duration of active inflammation, exclusive of relapses, averaged fourteen and one-half months but depended to a great extent on the age of the patient at the onset of illness: thirty-nine months for patients under 20 years and seven months for patients over 50 years of age. The duration of illness is the same for patients with positive and for patients with negative reactions to the Mantoux test. Of the 151 affected eyes, the inflammation became quiescent in 136, 56 of which subsequently had relapses. On the whole the relapses ran a mild course.

Of the total number of eyes, 63 per cent were left with good reading vision, and an additional 23 per cent had orientating vision. Operation for cataract was performed on 9 eyes. A severe relapse occurred in only 1 of these 9 eyes, while 5 had good reading vision and the rest orientating vision. In no case was the operation done until the eye had been quiescent at least a year.

One-half the patients presented roentgenographic changes in the lungs—about twice the average incidence. This, together with the favorable outcome of the treatment, is thought to lend support to the assumption of the tuberculous origin of iridocyclitis.

O. P. PERKINS.

HYPERPLASIA OF THE IRIS. L. BELIKOVA, *Vestnik oftal.* 25: 35, 1946.

A young soldier had impaired vision in the right eye due to chorioretinitis following trauma in childhood. Examination with slit lamp revealed two arches of trabecular tissue with holes about the pupillary region in each eye; these trabeculae had the structure of the normal stroma of the iris. The pupillary reaction was normal, and the case is reported because of this rare congenital anomaly.

O. SITCHEVSKA.

### Vision

EFFECT OF EXPOSURE TO SUNLIGHT ON NIGHT VISION. S. HECHT, C. D. HENDLEY, S. ROSS and P. N. RICHMOND, *Am. J. Ophth.* 31: 1573 (Dec.) 1948.

Hecht and his co-workers found that exposures to ordinary sunlight produced temporary and cumulative effects on night vision. They strongly recommend sunglasses transmitting 10 per cent or less of visible light for all persons who work in bright sunlight during the day and are then expected to perform critical night duties.

W. S. REESE.

## Book Reviews

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**Text-Book of Ophthalmology. Vol. IV.** By Sir W. Stewart Duke-Elder. Price, \$20. St. Louis: C. V. Mosby Company, 1949.

The long anticipated fourth volume of the "Text-Book of Ophthalmology" by Sir Stewart Duke-Elder has at last appeared with an apology for keeping us waiting because the author was for six years concerned with "matters outside the library." This volume is well worth the wait. It continues the now almost legendary influence the three previous volumes have had on ophthalmology in the English-speaking world.

If one reflects back to the period prior to the publication of volume I of this monumental work, it will be recalled that no ophthalmologist could be really well informed who did not have a reading knowledge of at least German and French. In order to cover the literature on any ophthalmologic subject, either in the basic sciences or in clinical subjects, one had to read the material in the original publication, and it was a most lamentable fact that this was seldom in the English language. With the appearance of Sir Stewart's text ophthalmologists were afforded for the first time a complete coverage of the world's ophthalmologic literature in English. In addition to being an excellent compilation of the literature, the material was assorted and evaluated with an amazingly astute comprehension of what was wheat and what was chaff.

In each new volume as it has appeared the material covered was exhaustively and authoritatively treated, so that most of us readily came to accept it as the last word on the subject. In more than one clinic in this country the three volumes are affectionately referred to as the "Bible," and without any loss of reverence for either work. There can be no doubt that these four volumes have revolutionized the teaching of ophthalmology in this country, and our debt to their author is beyond measure.

The present volume is entitled "The Neurology of Vision: Motor and Optical Anomalies." It is as comprehensive and beautifully executed as the previous volumes. The section on neurology starts with disorders of the visual pathways and their associated dysfunctions. This is followed by anomalies of the pupillary pathways, and, finally, the disturbances of the oculomotor apparatus are dealt with, including comitant squint and its associated sensory phenomena. In this systematic anatomic progression, the author covers the whole field of organic and functional pathology of the central nervous system as it finds expression in the eye. As in the previous volumes, the coverage of the world's literature seems to be complete, and the bibliography put at the end of each section saves considerable time when one wishes to refer to the original articles.

The last section of this volume covers the optical anomalies of the eye. Since the author has recently published the fifth edition of his "Practice of Refraction," this part of volume IV does not create the same excitement as the rest of the book, but not because it is of less value.

The style is the same as that which has characterized the other volumes in the set—lucid, and with a nice flow of words that satisfies one's sense of rhythm—and yet it is never verbose. It would make many of our publications more pleasant reading if Sir Stewart's style could be emulated. The paper, printing and, above all, the illustrations are superb. To the author of the present volume, and to all those who have contributed to its making, American ophthalmology owes a sincere debt of gratitude.

F. H. ADLER.

**Help Yourself to Better Sight.** By Margaret Darst Corbett. Price, \$2.50. Pp. 218. New York: Prentice-Hall, Inc., 1949.

The author was a pupil of the late William H. Bates and has been carrying out his teachings in her own Los Angeles School of Eye Education. If the results of this type of quackery were not so tragic, the book could be highly amusing. Chapter 9, for example, gives a summary of daily drills for *relaxation of the eyes, starting on page 42 with the following instructions:*

2. Yawn wide like a hippopotamus, dropping your chin, taking your head away from it and coming back to get it again. This loosens the lungs for deep breathing. There is nothing more effective than a yawn. Watch a dog or baby to perfect your skill.

3. Wiggle like a fish. Visualize the vertebral activity of a fish as it swims through the water. Try to imitate it by wiggling your own spine from the base of the skull down to the very last vertebra. Now your body is free.

In addition to such exercises as blinking and massaging the eyeballs, the author suggests brow wangling, which, she says, divorces the brows from the lid action.

FRANCIS H. ADLER, M.D.

**How to Become a Doctor.** By George R. Moon, A.B., M.A. Price, \$2. Pp. 131. Philadelphia: The Blakiston Company, 1949.

This book fills the need for some authentic instruction to students in college who are contemplating going into medicine or one of the allied professions, such as dentistry, pharmacy or occupational therapy. A list of the approved medical schools in the United States for 1948 is given together with their requirements for admission. There is a chapter on advice in selecting a medical school, as well as chapters on how to apply for admission and several chapters on the problems with which the medical student will find himself confronted. The book is highly recommended for any student considering entering the medical profession.

FRANCIS H. ADLER, M.D.

## ARNOLD KNAPP

The Editorial Board of the ARCHIVES OF OPHTHALMOLOGY felicitates Dr. Arnold Knapp on his eightieth birthday and wishes him many years of enjoyment in viewing the growing structure of ophthalmology in this country, which he influenced in such large measure. This issue represents in a small way the respect and affection which all ophthalmologists in this country and abroad have for him.

KNAPP BIRTHDAY VOLUME

This Issue of the  
Archives of Ophthalmology

Is Dedicated to  
DR. ARNOLD KNAPP  
On His Eightieth Birthday

*In Recognition of His Outstanding Contributions to Ophthalmology*

Committee for Knapp Birthday Volume

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ARNOLD KNAPP, M.D.



## FOREWORD

By dedicating this volume to Dr. Arnold Knapp on his eightieth birthday, his colleagues wish to express their esteem and affection for this distinguished ophthalmologist. Born into our specialty, the son of Dr. Herman Knapp, he not only has fostered the sound teachings of his illustrious father, but has greatly enriched ophthalmology by his own efforts. Having been reared in this scientific atmosphere, it is no wonder that he with his inquisitive mind soon became all-absorbed in its search for knowledge—a search that still goes on. Not contented with theories and speculation, he has always devoted his efforts to learning the truth and to stating it in clear words. The ability to winnow the chaff from the grain is an outstanding characteristic of this man. Soundness of judgment, clarity of expression and thorough knowledge of the subject are evidenced in all his writings. To acquire these traits has meant a life devoted unstintingly to study. Ophthalmology is his love, and he has nurtured her well.

After receiving his Bachelor of Arts degree from Harvard in 1889, he entered the Columbia University College of Physicians and Surgeons. Three years later this medical tyro started a surgical internship at Roosevelt Hospital, New York city, with the avowed purpose of becoming a general surgeon. To the loss of surgery and to our great gain, his interest shifted to ophthalmology. After a period of training in European clinics he became associated with his father in the practice of ophthalmology in New York. In these stimulating surroundings he worked assiduously and acquired great clinical experience. At the same time he assessed the pros and cons of his teaching and emerged, not a puppet, but an independent thinker.

The New York Ophthalmic and Aural Institute was the scene of his early activities. This hospital on the lower East Side of New York, which was started by his father in the same year that Arnold was born, was prospering well by the time he began practice. Its staff included Alexander Duane, Ward A. Holden, Charles H. May, H. H. Tyson and John E. Weeks, all distinguished ophthalmologists. Dr. Herman Knapp remained its guiding spirit until 1909, when he was forced to retire on account of ill health. After assuming the position of executive surgeon, Arnold Knapp soon culminated previous plans of his father for expansion of the hospital's facilities by moving into a newly constructed building on Fifty-Seventh Street and Tenth Avenue. With the opening of this institution, on Oct. 1, 1913, its founder was honored by having the name changed to the Herman Knapp Memorial Eye Hospital. In these new surroundings clinical work and postgraduate teaching continued. The scientific atmosphere prevailed, with emphasis on clinical rather than on research activities. After rendering great service to ophthalmology and humanity for over twenty-five years, it merged in 1940 with the Institute of Ophthalmology of the Presbyterian Hospital. With its assets a Knapp Memorial Foundation was created for the advancement of postgraduate study, teaching and research in ophthalmology under the auspices of Columbia University. This fund has supported many of the research activities of



the Institute of Ophthalmology, including the Knapp Research Laboratory, under the direction of Dr. Ludwig von Sallmann, and the Knapp Laboratory of Physiological Optics, with Dr. LeGrand H. Hardy in charge. These two laboratories bespeak the far-reaching interest Dr. Knapp has in scientific ophthalmology.

In 1911 he assumed the editorship of the ARCHIVES OF OPHTHALMOLOGY, which was founded in 1869 by his eminent father. For thirty-eight years he guided its destinies, and for this distinguished service ophthalmology owes him its greatest debt of gratitude. His devotion to its cause did more for the advancement of American ophthalmology than any other one man's efforts. Not only did he critically analyze the contents of each issue but also he added greatly to its prestige by contributing freely articles of his own. His presentations always contain sound clinical observations expressed in clear, concise terms. He not only writes well but edits well. His friendly criticisms of the literary efforts of his colleagues did much to elevate the standard of its articles. The enviable position in ophthalmologic literature held by this periodical is the result of his efforts. For this achievement ophthalmologists the world over salute him.

The arduous duties of this editorship have not deterred Dr. Knapp from assuming other responsibilities. In 1917 he published a volume on "Medical Ophthalmology," a subject which still remains dear to his heart. He has contributed many papers before local and national societies, and his interest continues unabated. His regular attendance at the meetings of the Section of Ophthalmology of the New York Academy of Medicine and the New York Ophthalmological Society is revealing of his love of ophthalmology, as is his frequent presence at the instruction courses given at the meetings of the American Academy of Ophthalmology and Otolaryngology.

For twenty-five years, from 1903 to 1928, he was professor of ophthalmology at Columbia University College of Physicians and Surgeons. On his retirement from active teaching he was appointed professor emeritus. In 1931, in recognition of this long and distinguished service, he was awarded an honorary degree of Doctor of Science by his alma mater. In 1941 the National Society for the Prevention of Blindness awarded him the Leslie Dana Gold Medal. The American Ophthalmological Society honored him with its presidency in 1931; the Section on Ophthalmology of the American Medical Association, with its chairmanship in 1925. In 1946 he delivered the Bowman Lecture before the Ophthalmological Society of the United Kingdom with a most comprehensive and thorough review on "The Present State of the Intracapsular Cataract Extraction." At this time he was elected an honorary member of that distinguished society.

These are but a few of the many honors that have been bestowed on this forthright, clear-thinking, illustrious gentleman, to whom ophthalmology is so much indebted. While we take just pride in his past accomplishments, we rejoice still more in the knowledge that his activities continue. May our debt of gratitude increase for many years to come.

JOHN H. DUNNINGTON, M.D.

THERAPEUTIC ACTION OF STREPTOMYCIN AND PROMIZOLE®  
IN CLINICAL OCULAR TUBERCULOSIS

A Preliminary Report

ALAN C. WOODS, M.D.

BALTIMORE

THE EXPERIMENTAL background for the use of both streptomycin and promizole® (4,2-diaminophenyl-5'-thiazolsulfone) in treatment of ocular tuberculosis has been presented in previous publications.<sup>1</sup> It was first pointed out<sup>1a</sup> that promizole® had a deterrent action on the course of ocular tuberculosis in the immune-allergic rabbit. This effect became evident after the third week of treatment. There were, however, both clinical and histologic evidences of active disease in the eyes of these treated animals, although much less than in the controls. In the next study,<sup>1b</sup> it was shown that the deterrent action in the normal rabbit, in which there was no immunity and the test therefore was much severer, was much less than in the immune-allergic animal. In the third study,<sup>1c</sup> the therapeutic actions of streptomycin and of the combination of streptomycin and promizole® in the immune-allergic rabbit with ocular tuberculosis were reported. Streptomycin alone had a highly deterrent action on the disease; nevertheless, minimal histologic evidences of active tuberculosis remained in the eyes of the treated animals. The combination of streptomycin and promizole®, however, produced a most dramatic therapeutic result. The eyes of all treated rabbits were free of all clinical evidence of activity after four weeks of treatment, and showed only scarring or the persistence of a few wandering cells on histologic examination. There was only 1 instance of relapse in the animals kept for observation after cessation

From the Wilmer Ophthalmological Institute of the Johns Hopkins Hospital and University.

Read at the Fifty-Fourth Annual Meeting of the American Academy of Ophthalmology and Otolaryngology, Chicago, October, 1949

1. (a) Woods, A. C., and Burky, E. L.: Studies in Experimental Ocular Tuberculosis: X. The Effect of "Promin" and "Promizole" in Experimental Ocular Tuberculosis in the Immune-Allergic Rabbit, *Arch. Ophth.* **39**:471 (April) 1948; (b) XI. Effect of "Promin" and "Promizole" in Experimental Ocular Tuberculosis in the Normal Rabbit, *ibid.* **40**:1 (July) 1948. (c) Woods, A. C., and Wood, R. M.: Studies in Experimental Ocular Tuberculosis: XII. Effect of Streptomycin and "Promizole" in Experimental Ocular Tuberculosis in the Immune-Allergic Rabbit, *ibid.* **40**:413 (Oct.) 1948.

of treatment. For 6 animals culture of the uveal tracts, only 1 showed tubercle bacilli, and on transmission experiments 50 per cent of the uveal tracts of the treated animals were noninfectious, while the uveal tracts of all the untreated controls showed positive cultures and were infectious. It was concluded that the combination of streptomycin and promizole® had a therapeutic action much greater than could be expected from mere summation and that this effect probably was due to a synergistic action—the two agents either attacking separate phases of the metabolism of *Mycobacterium tuberculosis* or different mutants of the organisms. In the most recent study,<sup>2</sup> it was shown that this combination of streptomycin and promizole® had an equally favorable therapeutic effect in the normal rabbit, indicating that the drugs acted entirely independent of immunity, and quite probably had a direct bactericidal effect on the bacilli.

With the demonstration of the dramatic therapeutic action of these agents in experimental ocular tuberculosis and their relative lack of toxicity in animals, the next step was to apply this form of therapy to ocular tuberculosis in human beings and to evaluate its therapeutic activity.

#### CHOICE OF PATIENTS

In the application of any form of supposedly specific therapy to ocular tuberculosis, one is always beset with the uncertain nature of the diagnosis. In the absence of tissue for biopsy and material for animal inoculation or from which the bacilli may be isolated, the diagnosis must perforce be presumptive. Therefore, in the evaluation of any new form of therapy, the diagnostic criteria should be unusually rigid.

There were two guiding principles in the choice of patients to be treated. The first principle was that the diagnosis of ocular tuberculosis in any treated patient must be so firm that it would meet the approval of an experienced ophthalmologist. The diagnostic criteria observed were as follows: (a) The ocular disease must conform to a pattern commonly regarded as tuberculous, and one in which histologic examination of eyes with similar disease patterns had uniformly demonstrated the probable tuberculous nature of the disease; (b) the patient must show elsewhere in the body evidences of a preceding tuberculous infection, a source from which the ocular infection might logically have arisen; (c) the cutaneous reactions to tuberculin must be in conformity with those for the patient's age and tuberculous status, and (d) the most thorough and exhaustive medical survey possible should reveal no

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2. Woods A. C., and Wood, R. M.: Studies in Experimental Ocular Tuberculosis: XIII. Effect of Streptomycin and Promizole on Experimental Ocular Tuberculosis in the Normal Rabbit, to be published.

other systemic disease or cause to which the ocular inflammation could logically be attributed. The details of this diagnostic survey have been outlined elsewhere.<sup>3</sup> The second guiding principle in the selection of patients was that the ocular disease either had not yielded to more conventional forms of therapy or did not appear amenable to such therapy and that the condition of the patient was sufficiently desperate to warrant any risk that this treatment might entail.

Thirteen of the 14 patients whose cases are reported here met these criteria. In 1 case (10) the decision to treat the patient was borderline. While the clinical picture was highly suggestive and the diagnostic survey revealed no probable cause other than tuberculosis, the patient's reactions to tuberculin were almost negative and the only evidence of previous systemic infection was a calcified nodule in the lower lung field. This patient was treated only after consultation with the referring physician on the premise that the diagnosis was more than usually presumptive.

The 14 patients treated with streptomycin and promizole® may be grouped as follows: Three had generalized uveitis, 1 with concomitant scleritis; 4 had classic sclerokeratitis, all with anterior scleritis and pronounced corneal involvement; 1 had diffuse scleritis, both anterior and posterior, with proptosis and limitation of movement of the eye; 4 had severe exudative choroiditis, all with some involvement of the anterior ocular segment with mutton fat keratic deposits and Koeppe nodules, and 2 had hemorrhagic retinitis, or Eales's disease. As already stated, all but 1 of the patients (case 10) appeared to be tuberculous beyond shadow of any reasonable doubt, and there was little probability that any ophthalmologist would have made any other diagnosis in her case.

#### EVALUATION OF RESULTS

In the evaluation of results, it must be remembered that each observation of a therapeutic response is entirely uncontrolled. In the experimental disease, each treated rabbit is controlled by a rabbit of similar breed, inoculated in a precisely similar manner and maintained under identical conditions. In such controls the course of the untreated disease can be carefully followed, evaluated and compared with the course of the disease in the treated animal. At the end of treatment, tissue is available for histologic examination, culture and transmission experiments. In the human subject no such controls are possible. The judgment of the observing physician that the individual patient under treatment did better than would have been expected in the natural course of events and the summation of such judgments for a number

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3. Woods, A. C.: The Etiological Diagnosis of Uveitis, Monograph of the American Academy of Ophthalmology and Otolaryngology, to be published.

of patients is the only method of assaying the value of the therapeutic agents. Thus, the value of any observation is directly proportional to the individual ophthalmologist's knowledge of, and experience with, ocular tuberculosis. This, of course, introduces the human equation.

A second difficulty in evaluating a therapeutic response is the known tendency of ocular tuberculosis to undergo exacerbations and remissions and the resulting difficulty of attributing an improvement to the action of the therapeutic agent. Here, again, it is largely a matter of study and opinion, although the time relation of clinical improvement to the administration of the therapeutic agents may clearly indicate a cause and effect relationship. In the cases here reported the time of the onset of any improvement in relation to the beginning of therapy and the continuity of improvement was carefully considered.

A third difficulty is that a careful distinction must be made between reversible and irreversible changes in the eye. All any therapeutic agent can do is to destroy or immobilize the causative organism of the disease. If the disease is still in the infiltrative stage and tissue destruction or permanent inhibition of nutrition has not occurred, the destruction or fixation of the causative agent will be followed by a return of function. However, if irreversible changes have already taken place, little or no improvement in function can be expected. Among such irreversible changes in the eye would be the presence of corneal scars; the existence of organic adhesions with their destructive sequelae; interference with the nutrition of the lens with resultant incipient cataract, which may reasonably be expected to progress to maturity even though the underlying disease is controlled; the presence of heavy vitreous opacities, which may shrink over a long period but are, nevertheless, more or less permanent, and the actual destruction of the pericipient elements of the retina with secondary gliosis. Therefore, at the beginning of therapy such organic changes should be carefully noted and estimated, and their persistence, after termination of therapy and the control of all inflammatory manifestations of the disease, should not be regarded as evidences of the failure of the therapeutic agent.

#### ADMINISTRATION OF THERAPEUTIC AGENTS

The proper dose and methods of administration of new agents are largely matters of clinical observation. Fortunately, with both streptomycin and promizole® considerable accurate information was already at hand. The report of the Veterans Administration to the Council of Pharmacy and Chemistry of the American Medical Association <sup>4</sup>

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4. The Effect of Streptomycin on Tuberculosis in Man, Report of the Council on Pharmacy and Chemistry, J. A. M. A. **135**:634 (Nov. 8) 1947. Dosages of Streptomycin in Tuberculosis, Current Comment, *ibid.* **133**:842 (Nov. 29) 1947.

showed that in man equally good therapeutic effects with streptomycin were obtained when the antibiotic was given in doses of 0.5 Gm. every twelve hours as when similar doses were given every six hours or oftener. Further, with this dose the toxic effects were considerably less, involvement of the vestibular branch of the eighth nerve occurring in only 17 per cent of persons so treated, whereas it occurred in 96 per cent of patients receiving 2.0 Gm. or more a day. This finding of a similar therapeutic response to smaller doses given at greater intervals is also in conformity with Feldman's experimental results.<sup>5</sup> As concerns promizole,<sup>®</sup> it had been found that a satisfactory therapeutic response was achieved in experimental animals with blood levels of from 1.5 to 2.0 mg. per hundred cubic centimeters, and this observation had been confirmed in cases of human systemic tuberculosis in which a similar treatment was given. Blood levels of this magnitude are readily obtained in man by the administration of 6 Gm. of promizole<sup>®</sup> a day in divided doses. In the light of this information, these doses were adopted for the treatment of ocular tuberculosis in the patients here reported, i. e., 0.5 Gm. of streptomycin administered intramuscularly every twelve hours and 6.0 Gm. of promizole<sup>®</sup> given orally in divided doses. With this dosage, the promizole<sup>®</sup> level of the plasma varied from 1.2 to 2.5 mg. per hundred cubic centimeters. Since these doses gave a minimum of toxic reactions combined with an eminently satisfactory therapeutic response, they were in general given to all patients, with 2 exceptions (cases 12 and 13). The newer dihydrostreptomycin hydrochloride was used in treatment of the last 7 patients, with an equally favorable therapeutic response. In passing, it may be noted that recent unpublished reports do not indicate a lessened toxicity of this preparation, but, rather, demonstrate a deferred toxic action. It is worthy of note, however, that 1 patient in this series (case 8) who had previously abandoned streptomycin therapy on account of evidences of vestibular irritation was later able to take the dihydro salt without any toxic symptoms.

To the first patient treated, streptomycin was first given alone, and promizole<sup>®</sup> was added only two weeks before cessation of the streptomycin therapy. This patient was treated before the synergistic action of the two agents had been demonstrated, and therapy was planned with the idea that the promizole<sup>®</sup> would be continued after a full course of treatment with streptomycin (120 Gm.). To the second patient, promizole<sup>®</sup> alone was given for a period of seven months, and streptomycin was added only when the patient had an exacerbation.

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5. Feldman, W. H.; Hinshaw, C. H., and Karlson, H. G.: Frequency of Administration of Streptomycin: Its Influence in Results of Treatment of Tuberculosis in Guinea Pigs, *Am. Rev. Tuberc.* 55:435 (Oct.) 1947.

To all other patients, streptomycin and promizole® were given synchronously, and the combination was continued until what was considered a "full course" had been given or the occurrence of toxic symptoms indicated that one or the other agent should be withdrawn.

The total proper doses of streptomycin and promizole® for ocular tuberculosis are still undetermined both in experimental animals and in man. On the basis of the information gleaned from experimental observations, and the published clinical reports on the amounts of streptomycin used in treatment of systemic human tuberculosis, it was first decided that a "full course" of streptomycin for ocular tuberculosis in man would be equivalent to a dose somewhere between 120 and 200 Gm. Inasmuch as definite clinical improvement was noticed after the administration of much smaller amounts, and one was naturally fearful of vestibular damage with the prolonged use of streptomycin, it was decided to cut the total dose of streptomycin first to 65 Gm. and later to 42 Gm. if these amounts could be taken without toxic symptoms. Certainly, satisfactory immediate clinical results were obtained with as little as 26 Gm. of streptomycin combined with 156 Gm. of promizole®, but whether or not these results will be permanent, or whether the patient will later show recurrences, remains to be seen. For the present, until more information is available, it would appear that when streptomycin is given with promizole® a total dose of 42 Gm. of streptomycin given in doses of 0.5 Gm. twice daily would be sufficient in all but especially severe and resistant cases. As far as promizole® is concerned, the drug is relatively nontoxic in doses of 6 Gm. a day. When toxic symptoms appear, they are quite definite—fever, vertigo, anorexia, malaise, leukopenia and dermatitis—and they disappear immediately on withdrawal of the drug. Therefore if the drug is being well tolerated, and there appears to be any clinical indication for its further use, there is little reason that it should not be continued after the course of streptomycin is completed. However, in the cases here reported, a total of 250 Gm. appeared adequate, although many patients took far greater amounts. It might be noted that a red color of the urine is the rule in promizole®-treated patients and should not be considered a toxic reaction.

#### RESULTS

The pertinent data on the cases and the therapeutic results are given in the accompanying table. Summaries of the 14 case histories are presented at the end of the paper.

*Therapeutic Response.*—In all of the 14 cases here reported there was complete resolution of all inflammatory symptoms. In 1 instance (case 12) the patient arbitrarily reduced the dose of streptomycin to

0.5 Gm. once a day, and the condition did not completely clear up with this dose. However, when the dose was increased to 1.0 Gm. a day there was complete clearing in three weeks.

The first evidence of change for the better was observed from nine days to three weeks after the beginning of treatment, and the improve-

*Data on Treatment of Patients with Ocular Tuberculosis with Streptomycin and Promizole®*

No.	Age, Yr.	Diagnosis	Duration and Amount of Treatment		Toxic Reactions		Results
			Streptomycin	"Promizole"	Streptomycin	"Promizole"	
1	55	Scleritis, uveitis	5 mo. 120 Gm.	3½ mo. 676 Gm.	+	+	Complete subsidence of all inflammation; mature cataract
2	48	Choroiditis	42 days 42 Gm.	17 mo. 2,250 Gm.	+	None	Complete subsidence of choroiditis; vision improved from 20/100 to 20/30+
3	38	Uveitis	34 days 34 Gm.	8 mo. .....	+	None	Complete subsidence of all inflammation; mature cataract
4	55	Bilateral sclerokeratitis	30 days 39 Gm.	16 days 98 Gm.	None	+	Complete subsidence of inflammation; vision rose from 1/200 to 8/200
5	26	Choroiditis	6 wk. 80 Gm.	6 wk. 300 Gm.	None	None	Complete resolution of choroidal exudate; vision rose from 10/200 to 20/30
6	56	Uveitis	5 mo. 152 Gm.	5 mo. 900 Gm.	None	None	Complete subsidence of all inflammation; mature cataract
7	49	Bilateral sclerokeratitis	26 days 26 Gm.	26 days 156 Gm.	Slight	Slight	Subsidence of inflammation; no change in vision
8	48	Choroiditis	37 days 37 Gm.	60 days 450 Gm.	None	None	Subsidence of inflammatory symptoms; vision rose from 3/200 to 12/200
9	61	Sclerokeratitis	65 days 65 Gm.	31 days 252 Gm.	None	+	Complete subsidence of all inflammation; vision rose from counting fingers to 20/20 —1
10	24	Choroiditis	42 days 42 Gm.	42 days 252 Gm.	None	None	Presumptive diagnosis; arrest of progression and subsidence of inflammatory symptoms; no change in vision
11	24	Scleritis	40 days 40 Gm.	67 days 400 Gm.	None	None	Complete subsidence of all inflammation; vision rose from 20/30 to 20/20
12	24	Sclerokeratitis uveitis	112 days 84 Gm.	91 days 504 Gm.	None	+	Regression of original lesions and improvement of vision from 20/100 to 20/40; one area of scleritis persisted after administration of 63 Gm. but cleared completely after a total dose of 84 Gm.
13	37	Hemorrhagic retinitis	42 days 168 Gm.	42 days 252 Gm.	None	None	Absorption of hemorrhages; vision in right eye rose from 1/200 to 20/100; vision in left eye improved from 20/50 —1 to 20/40
14	31	Tuberculous periphlebitis of retina	42 days 42 Gm.	42 days 252 Gm.	None	None	Absorption of hemorrhages; vision in right eye rose from finger counting to 20/30; vision in left eye declined from 30/50 to finger counting and then improved to 6/200 on discharge

ment steadily continued after cessation of treatment until the eyes showed no evidences of any activity. However, irreversible changes did not disappear; vitreous opacities remained, although vitreous haze cleared and the opacities became more circumscribed (cases 2 and 8). In 3 cases (1, 3 and 6) lenticular opacities already well advanced when treatment was started progressed steadily until the cataracts became mature. In cases 4 and 7; with heavily scarred corneas, there were



no changes in vision, although all evidences of inflammation disappeared. These cases may all be taken as instances of irreversible changes in the eye. In all the remaining cases there was not only complete clearing of all clinical evidences of active inflammation but also a considerable restoration of vision. This varied from a minimum improvement of from 3/200 to 12/200, with irreversible opacities in the vitreous, in case 8, to a maximum improvement of from finger counting at 2 feet (60 cm.) to 20/20 — 1, in case 9. In the latter case the initial visual loss was due to early, unorganized infiltrates in the cornea, a reversible change.

The conspicuous finding in relation to the therapeutic response was the uniform, and apparently complete, control of the clinical evidences of inflammation. In the limited period of observation after cessation of treatment there have been no recurrences. The period of observation, however, has been too short to justify any conclusion on this point. However, the indications, from the evidence at hand, are that these agents have a therapeutic action in human ocular tuberculosis quite comparable to their effect in experimental animals—certainly a bacteriostatic, and probably a bactericidal, effect.

*Toxic Reactions.*—Streptomycin: All patients given streptomycin were warned of the possibility of vestibular symptoms and were instructed to discontinue use of the drug on the appearance of any vertigo. Patients under immediate control were examined each week by an otolaryngologist for any evidences of vestibular irritation, and patients not under immediate control were instructed to have similar examinations made by their local specialists.

In 4 cases (1, 2, 3 and 7) evidences of vestibular irritation developed with streptomycin therapy. In 1 case symptoms developed with streptomycin, but the patient later took dihydrostreptomycin without reaction. In every case the symptoms disappeared after the drug was withdrawn. There was no instance of any residual damage to the vestibular tract and no persisting aural symptoms. With the precautions of warning the patient, weekly aural examinations and immediate withdrawal of the antibiotic on any evidence of vestibular irritation, there appears to be no significant danger in the use of streptomycin.

Promizole®: In 4 cases (1, 4, 9 and 12) definite toxic reactions to promizole® occurred. In case 1 the patient took 600 Gm. of promizole® without reaction over a three and one-half month period and then exhibited weakness and malaise. The icterus index was found to be 17.2. Promizole® was discontinued, and there was prompt recovery. Two weeks later the patient recommenced use of the drug and then took 76 Gm., without symptoms. She then again complained of weak-

ness and dizziness. The icterus index at this time was 12, and the result of the Hanger flocculation test was positive. Promizole® was then permanently discontinued, with prompt recovery from all toxic symptoms. In case 4 dermatitis developed; this subsided when promizole® was withdrawn and recurred when it was again given. Patient 9 was hospitalized in the Wilmer Institute during treatment. After receiving 140 Gm. of promizole®, she had an unexplained fever and relative leukopenia. Promizole® was stopped, with prompt disappearance of all symptoms. Fever and leukopenia recurred when promizole® was again given, after a week's rest. The drug was then permanently discontinued, with prompt subsidence of the fever and a rise in the white cell count to normal. In case 12 relative anemia and leukopenia developed after administration of 500 Gm., and the drug was permanently discontinued. In another case (7) the patient experienced slight symptoms, consisting of lassitude, headache and anorexia, after taking 156 Gm. of promizole®. Symptoms promptly disappeared after withdrawal of the drug, and promizole® was not again given. The occurrence of toxic reactions to promizole® did not appear to be related to any undue concentration of the drug in the plasma. Similarly, there was no indication of undue retention of the drug, the maximum plasma level obtained being 2.8 mg. per hundred cubic centimeters. In all other cases promizole® was administered without symptoms of any kind, and in 1 case (2) the patient continues to take small daily doses as a precautionary measure and has now received a total of over 2,000 Gm.

*Relation of Toxic Symptoms to Total Dose.*—Streptomycin: In no case was evidence of vestibular irritation noticed until a minimum total dose of 26 Gm. had been reached. Other total doses for patients showing toxic symptoms were 34, 42 and 120 Gm. In all cases in which reactions occurred, the clinical improvement preceded the occurrence of the toxic symptoms. Thus, in case 7, with the minimum dose of 26 Gm. combined with 156 Gm. of promizole®, an excellent therapeutic response had been obtained before any toxic symptoms appeared.

Promizole®: The patients showing reactions to promizole® received from 98 to 600 Gm. before any toxic symptoms were noted. In each of these patients there had already been a satisfactory response to the treatment, which continued after the drug was withdrawn.

The evidence so far amassed indicates that while toxic reactions occur in a large percentage of patients treated with streptomycin and promizole®, in no instance so far observed have the symptoms been severe or followed by any permanent residua. Moreover, in all instances the toxic symptoms were delayed and did not occur until a satisfactory therapeutic response had been obtained. It would appear therefore that with proper precautions the combined treatment with streptomycin

and promizole® is reasonably safe. Since toxic reactions appear to be delayed, a therapeutic response may be expected before any toxic manifestations occur.

#### COMMENT

The cases here reported represent my total personal experience with the treatment of clinical ocular tuberculosis with streptomycin and promizole® up to July 27, 1949. The small number of patients treated is explained by the rigidity of the criteria for selection, namely, that the primary diagnosis be almost unquestioned and that the condition be of sufficient seriousness to justify treatment. The number of cases is admittedly too few, and the period of post-treatment observation too short, to permit valid conclusions. This report must therefore be considered a preliminary one. However, the material at hand does indicate a remarkable therapeutic effect for the combination of streptomycin and promizole® in clinical ocular tuberculosis—namely, that toxic reactions are frequent but are comparatively mild, and that there is a reasonable expectancy for a therapeutic response before any toxic reactions become manifest. In short, there appears to be sufficient evidence for a more widespread use of these agents in treatment of tuberculosis of the eye.

A more widespread use must of necessity be followed by some unfavorable reports. There is no evidence whatsoever that these preparations are of the slightest value in any forms of endogenous ocular disease other than those caused by *Mycobacterium tuberculosis*. The difficulty in establishing a diagnosis of ocular tuberculosis has been mentioned here and explored at length elsewhere. Both the clinical and the experimental forms of ocular tuberculosis mimic the changes produced by other granulomatous diseases—syphilis, brucellosis, sarcoidosis, virus diseases, fungous disease—to an amazing degree. Since it is virtually impossible to establish conclusively the diagnosis of ocular tuberculosis by clinical examination alone, the most thorough and exhaustive medical survey is necessary to confirm the clinical impression. Even with such a complete survey, the final diagnosis is often somewhat uncertain. Therefore, it follows that if these agents obtain any widespread use by ophthalmologists, there is the probability they may be used for the treatment of other than tuberculous ocular disease. If the disease fails to respond to treatment, the failure will probably be attributed to the ineffectiveness of the therapeutic agents, although it may in truth be the result of an incorrect original diagnosis. The meager evidence at hand indicates that the absence of a therapeutic response to these agents in a case of supposed ocular tuberculosis might argue against the tuberculous nature of the disease, just as failure to respond to arsphenamine or penicillin argues against a syphilitic etiology. However, the available

evidence for absolute specificity in ocular tuberculosis is still too slight to warrant such a sweeping assumption. Further, it has been demonstrated that some strains of *Myco. tuberculosis* are naturally resistant to streptomycin. At present, the wisest course would be to limit the use of these preparations to frank or probable cases of ocular tuberculosis, and not to use them in cases of doubtful etiology. Only by this means can a respectable body of evidence for or against their efficacy be accumulated. All that can be said at this time is that streptomycin and promizole® have a proved and remarkable therapeutic effect in experimental ocular tuberculosis both in the immune-allergic and in the normal animal, and that the meager evidence at hand indicates a no less dramatic effect in ocular tuberculosis in man.

### CONCLUSIONS

1. Streptomycin given in doses of 0.5 Gm. twice daily combined with promizole® in the amount of 6 Gm. a day in divided doses had a dramatic effect in controlling the clinical evidence of activity and inflammation in the 14 patients with frank ocular tuberculosis so treated.

2. A therapeutic response was observed after nine to twenty-one days of treatment. The response thereafter was slow but steady.

3. Irreversible changes, such as corneal scarring, cataracts, vitreous opacities and organic tissue damage, were not influenced by such treatment. Reversible changes—corneal infiltrates, nodules in the iris, choroidal exudates and all inflammatory changes—regressed.

4. Toxic symptoms appeared in a large percentage of patients so treated. These symptoms were not serious and, if the drugs were discontinued, promptly disappeared without residua.

5. A therapeutic response was manifest before the appearance of any toxic manifestations.

### SUMMARY OF CASES

The protocols of the 12 cases are briefly summarized.

CASE 1 (referred by Dr. Charles Young).—A white woman aged 50 was first seen in May 1945. The family history was noncontributory, and the past history was also unremarkable except for a mastectomy in 1933. On admission she presented generalized granulomatous uveitis and scleritis in the right eye, the left eye being normal. Medical survey at that time was essentially noncontributory except for a pronounced hypersensitivity to tuberculin. She was placed under tuberculin therapy, but it proved almost impossible to desensitize her on account of systemic and focal reactions. The condition of her right eye became steadily worse, and in 1946 the eye was enucleated as blind, painful and phthisical. Histologic examination showed diffuse tuberculous uveitis. Uveitis and scleritis developed in the left eye in 1946. Despite nonspecific treatment and administration of as much tuberculin as could be tolerated, the disease progressed; and in October 1947 there were advanced uveitis and scleritis with lenticular opacities and the

prognosis appeared almost hopeless. Streptomycin was given over a five month period, the total dose being 120 Gm. Its use was discontinued on account of toxic symptoms. Treatment with promizole® was started two weeks before cessation of streptomycin and was continued for three months, the total dose being about 600 Gm. Toxic symptoms then developed, and promizole® was discontinued. However, while the patient was still under treatment with streptomycin the eye began to clear, and improvement thereafter was steady, until in December 1948 there was no trace of inflammation. The lenticular opacities, present when first seen, progressed to a mature cataract, which was successfully removed on July 11, 1949.

CASE 2 (referred by Dr. M. E. Randolph).—A white physician aged 45 was first seen in December 1947. The family and past histories were noncontributory. Vision in the right eye had begun to fail two months previously. Examination showed extensive choroiditis in the temporal portion of the fundus with definite evidences of involvement of the anterior uvea. The left eye was normal. The medical survey was entirely noncontributory except for roentgenographic evidence of old extensive pulmonary tuberculosis. There was pronounced hypersensitivity to tuberculin. The condition became progressively worse despite nonspecific protein therapy and local diathermy. Vision was reduced to 20/100. The patient was placed first under treatment with promizole® alone, and the condition slowly improved for seven months, vision rising to 20/30. There was a sharp relapse after seven months' treatment with promizole® alone, and streptomycin was then added, followed by a prompt response after three weeks' treatment. Use of streptomycin was continued for forty-two days and then abandoned on account of vestibular irritation. Promizole® therapy was continued on a reduced dose of 4 Gm. a day. By December 1948 the choroiditis was quiet, and on April 1, 1949 vision was 20/30 + and there were no evidences of any activity. The anterior uvea appeared entirely normal. The patient continues to take promizole® as a precautionary measure. The total dose of streptomycin was 42 Gm. and the total dose of promizole® is now over 2,000 Gm.

CASE 3.—A white woman aged 30 was first seen in 1941 with exudative choroiditis of the left eye. Medical survey showed evidence of old pulmonary tuberculosis and violent hypersensitivity to tuberculin; otherwise it was noncontributory. The initial attack of choroiditis quieted under tuberculin therapy, which was discontinued after ten months; but four years later tuberculin was again given over an eight month period for a recurrence in cutaneous sensitivity without ocular recurrence. There was a recurrence of choroiditis in January 1948. Tuberculin therapy was again recommended. The patient apparently received excessive doses, and violent focal reactions ensued. She was seen again in March 1948. At that time there was violent active generalized uveitis of the left eye with reduction of vision to finger counting at 2 feet (60 cm.). The lens was opaque. Streptomycin and promizole® were given. The streptomycin was continued for thirty-four days (34 Gm.) and then discontinued on account of vestibular irritation. Promizole® was continued for eight months, the total dose being 1,410 Gm. There was a steady and complete subsidence of all inflammation. There was no improvement of vision, and on last examination, in April 1949, the eye was white and free of all inflammation, tension was normal and there was a mature cataract. Vision was reduced to light perception and good projection. The right eye remained normal.

CASE 4 (referred by Dr. Angus MacLean).—A white woman aged 55 was first seen in May 1948. The family and past medical histories were noncontributory.

The patient gave a history of recurrent bilateral sclerokeratitis since the age of 13 years. She had received tuberculin therapy over a fourteen month period in 1943-1944, with some beneficial results. On examination, the process in the right eye appeared inactive with old corneal scars, and the left eye showed a highly active sclerokeratitis and old scars. Vision was reduced to 1/200. The medical survey was again entirely noncontributory except for pronounced hypersensitivity to tuberculin and roentgenographic evidence of old, inactive pulmonary tuberculosis. Treatment with streptomycin and promizole® was started on June 2, 1948 and was continued for one month, the promizole® being discontinued because of dermatitis, which cleared when promizole® was withdrawn and recurred when it was again given. The total dose of streptomycin was 42 Gm., and the total dose of promizole®, 98 Gm. Subjective improvement was striking from the beginning of treatment; the examining ophthalmologist reported that monthly examinations showed excellent clinical improvement, subsidence of inflammation and clearing of corneal infiltrates. By November the eye was white and the disease inactive. Vision had risen to 8/200. The old corneal scars were unaffected.

CASE 5 (referred by Dr. Angus MacLean).—A white man aged 26 was first seen in October 1948. The family and past medical histories were noncontributory. In 1944 both eyes had been the site of repeated attacks of choroiditis, which had spared the macula. He had received tuberculin for three years, from 1945 to 1947, but was able to tolerate only low doses. In April 1948 a small exudative choroidal lesion developed in the left eye just nasal to the macula; this lesion cleared quickly, leaving the eye with 20/15 vision. There was recurrence in the left eye in August, and the eye did not yield to nonspecific protein or tuberculin therapy. When examined in October, the right eye showed scars of old inactive choroiditis and 20/20 vision. The left eye showed atrophic scars from the former attacks and a large active exudative lesion in the macula. Vision was reduced to 10/200, eccentrically. The medical survey was noncontributory except for extreme hypersensitivity to tuberculin and roentgenographic evidences of an inactive pulmonary lesion. Combined treatment with streptomycin and promizole® was started on Oct. 27, 1948 and continued until the patient had received a total of 80 Gm. of streptomycin and 300 Gm. of promizole®. Definite clinical improvement was noted two weeks after onset of treatment. The improvement steadily continued, and at the end of the seventh week the choroidal infiltrates had subsided. On last examination the eye appeared free of all evidence of active disease, showing only old pigmented scars. Vision had risen to 20/30, from the initial low of 10/200.

CASE 6.—A white woman aged 56 was first seen in June 1948. The family and past histories were noncontributory. Visual symptoms first developed in the left eye in November 1947. Examination in June 1948 showed that the right eye was normal throughout and revealed extensive exudative choroiditis in the left eye, with Koeppe nodules, mutton fat keratic deposits and mild evidence of involvement of the anterior uvea. Vision was reduced to perception of hand movements. Opacities were noted in the posterior cortex of the lens. A complete medical survey was noncontributory except for roentgenographic evidences of old pulmonary tuberculosis and a moderate sensitivity to tuberculin (0.1 mg.), compatible with her age. She was placed under treatment with streptomycin and promizole® on Aug. 21, 1948, and this treatment was continued steadily except for a twelve day remission (November 23 to December 5). On December 14, after 102 Gm. of streptomycin and 600 Gm. of promizole® had been given, the inflammatory signs in the anterior uvea had completely disappeared. Treatment was

continued until Feb. 4, 1949, the total dose of streptomycin being 152 Gm. and the total dose of promizole® 900 Gm. In February 1949 the eye was entirely quiet; there was no sign of any inflammatory reaction, but the cataract noted on first examination had slowly matured. Vision was reduced to light perception and good projection.

CASE 7.—A white woman aged 49 had been under observation for recurrent bilateral sclerokeratitis since 1931. The family history was noncontributory, and the past history was also without significance except for a pulmonary lesion in girlhood and a history of recurrent bilateral sclerokeratitis since the age of 17. On first examination (1931) vision was 20/50 in the right eye and 20/15 in the left eye. Both eyes showed pronounced peripheral scarring of the cornea, and there was active sclerokeratitis of the right eye. The medical survey was noncontributory except for roentgenographic evidence of inactive old pulmonary tuberculosis and pronounced hypersensitivity to tuberculin. The results of brucella studies were all negative in 1931 but became positive in 1945, when the patient had an unexplained intermittent fever. From 1931 to 1948 there were repeated attacks of sclerokeratitis in both eyes, especially the right. The patient received repeated courses of tuberculin, followed by ocular improvement, but complete desensitization to tuberculin could never be attained. Local diathermy and nonspecific protein therapy had no effect on the ocular inflammation. There was transient improvement under beta irradiation. In October 1947 a severe attack occurred in the right eye, and the condition did not respond to any form of therapy. By August 1948 vision was reduced to light perception and the condition of the eye was so critical that enucleation was considered. Treatment with streptomycin and promizole® was started on Aug. 10, 1948. Within two weeks improvement was noticeable and continued steadily thereafter. All treatment was stopped on Sept. 6, 1948 because of mild vestibular irritation and toxic symptoms. The patient received a total of 26 Gm. of streptomycin and 150 Gm. of promizole.® The improvement continued steadily after cessation of treatment, and by October 1948 the eye was free of any active inflammation. There was no visual improvement because of heavy corneal scarring. There have been no recurrences in a ten month period of post-treatment observation. Degenerative calcareous deposits have occurred in the cornea.

CASE 8 (referred by Dr. Arnold Knapp).—A white woman aged 48 was first seen in December 1948. The family history was noncontributory. There was a past history of cervical adenitis as a child and of a circumscribed choroidal lesion in the right eye ten years previously, the latter healing under tuberculin therapy. The present illness began in August 1948; it was characterized by severe recurrence of the choroiditis in the right eye with evidence of involvement of the anterior uveal tract. Penicillin and nonspecific protein therapy were given, without avail. Streptomycin and promizole® therapy had been given in New York over a twenty-three day period, without apparent improvement, and was discontinued on account of toxic symptoms. Examination in December 1948 revealed extensive granulomatous uveitis of the right eye with reduction in vision to 3/200; no fundus details were visible on account of the clouding of the vitreous. The medical survey in New York and Baltimore was noncontributory except for roentgenographic evidences of an old inactive tuberculous lesion in the right outer lung field and pronounced hypersensitivity to tuberculin. Dihydrostreptomycin was now given with promizole,® the combined therapy being started on Feb. 14, 1949 and continued for thirty-seven days, without toxic reaction. Treatment was followed at

this time by clearing of all signs of inflammation of the anterior segment, relative clearing of the vitreous to the point where the fundus could be dimly seen and increase of vision to 12/200. Mild transient secondary glaucoma had developed. The total streptomycin dose was 60 Gm., and that of promizole,<sup>®</sup> approximately 480 Gm.

CASE 9.—A Negro woman aged 61 was first seen in February 1949. The family and past histories were noncontributory. The present illness was an inflammation of the right eye since August 1948. Examination showed violent sclerokeratitis of the right eye with vision reduced to finger counting at 2 feet. The medical survey showed extensive healed calcified pulmonary tuberculosis and violent hypersensitivity to tuberculin. All other examinations, including biopsy of a lymph node, revealed nothing abnormal. Treatment with streptomycin and promizole<sup>®</sup> was started Feb. 21, 1949. Promizole<sup>®</sup> was discontinued on March 22, 1949 on account of toxic symptoms (fever), but streptomycin was continued until April 25. The total dose of streptomycin was 65 Gm., and that of promizole,<sup>®</sup> 180 Gm. The eye steadily improved, inflammation subsided, the keratic precipitates became crenated, the cornea cleared and vision rose to 20/40 on the patient's discharge, on April 25. On May 24 the eye was entirely inactive and free of all inflammation; vision was 20/20—1, and there was one small scar remaining in the cornea.

CASE 10 (presumptive case, referred by Dr. Julius M. Dan).—A white woman aged 24 was first seen March 8, 1949. The family history was noncontributory. The only suggestive finding in the past history was a fistula-in-ano several years previously. Peripheral chorioretinitis developed in the right eye in January 1949; the condition did not yield to penicillin therapy, local treatment or general nonspecific therapy. Examination showed heavy vitreous opacities and some subretinal edema, but no areas of frank exudation. There were numerous Koepe nodules and heavy mutton fat keratic deposits. Vision was 20/50. The left eye showed keratic precipitates but had 20/20 vision, and no lesions were present in the fundus. Medical survey was noncontributory throughout except for the presence of a calcified nodule in the left lower lung field. The patient was relatively insensitive to tuberculin. A presumptive diagnosis of tuberculous choroiditis was made and the patient placed under therapeutic trial with dihydrostreptomycin and promizole.<sup>®</sup> This treatment was continued over a forty-two day period, the total dose of streptomycin being 42 Gm. and the dose of promizole<sup>®</sup> 252 Gm. On June 17, her referring ophthalmologist reported vision of 20/50 in the right eye and 20/20 in the left eye. There were no evidences of any activity on ophthalmoscopic examination. The keratic precipitates either had been absorbed or were crenated. The vitreous opacities were unchanged. Her ophthalmologist summarized his findings as follows: "I feel that the treatment has been of definite benefit. The pathologic process in the eye was progressing up to the time treatment was started. There seems to be a halt in the advancing process."

CASE 11.—A Negro woman aged 24 was admitted to the Johns Hopkins Hospital on March 21, 1949 with a diagnosis of scleritis of the left eye. The family and past histories were noncontributory. Examination revealed that the right eye was negative throughout. The left eye showed a diffuse purplish red congestion, involving all the visible anterior portion of the sclera. There were relative proptosis of the eye and almost complete immobility of the eye. The aqueous ray was present. Vision was 20/20. A diagnosis of deep scleritis, both anterior and posterior, with secondary tenonitis, was made. The medical



survey was essentially noncontributory except for roentgenographic evidences of old pulmonary tuberculosis and moderate sensitivity to tuberculin. She was placed under treatment with streptomycin and promizole® for a period of forty days, and promizole® therapy was continued alone for a further period of twenty-nine days. The total dose of streptomycin was 40 Gm., and that of promizole®, 402 Gm. Notable improvement was noted after fourteen days' treatment. At the end of three weeks the proptosis had disappeared and there was good motility. At the end of the sixth week there remained only slight congestion of the sclera, and at the end of the tenth week there was a complete symptomatic cure, with subsidence of all evidences of scleritis and other inflammation.

CASE 12 (referred by Dr. Luther C. Brawner).—A white woman aged 24 was first seen March 22, 1949. The family history was interesting. Her mother and father had died of tuberculosis, and one brother had active tuberculosis. Her past medical history was essentially noncontributory. She had had repeated attacks of sclerokeratitis in the right eye over a three year period. There had been intermittent tuberculin therapy for three years, with no effect. The left eye had become inflamed one month prior to examination. Examination of her eyes showed pericorneal inflammation of the right eye, with five areas of deep infiltration in the cornea; and ophthalmoscopic examination revealed a small pigmented, atrophic lesion above the macula. Vision was 20/100. The left eye was quiet but showed a paracentral corneal infiltrate and three marginal infiltrates. Vision was 20/15. There were no keratic precipitates in either eye. The medical survey showed violent hypersensitivity to tuberculin (0.001 mg.) and old tuberculous calcification in the left lung and paratracheal area. Treatment with streptomycin and promizole® was begun April 9. She received 1.0 Gm. daily for the first three weeks and thereafter only 0.5 Gm. daily. By May 24 she had taken 32 Gm. of streptomycin without reaction and 252 Gm. of promizole®. Definite clinical improvement was noticed early in May. On May 24 there was a notable lessening of the inflammation, there being only a suggestion of congestion remaining, and the infiltrates were decidedly less. Vision had improved from 20/100 to 20/50. However, four posterior synechias had formed, and there was a nodule-like mass in the stroma of the iris. Both streptomycin and promizole® were therefore continued to July 6, making the total dose of streptomycin 63 Gm. and that of promizole® 504 Gm. On July 6 the patient's physician reported that in the interim there had been temporary vascularization of the cornea, which had regressed. Examination revealed that vision was 20/50; the cornea was clear, except for interstitial scars; there were no keratic deposits, and the aqueous ray was absent. The iris was free of inflammation; there were no nodules. The posterior synechias were still present. There was, however, an area of scleritis at the extreme temporal sclera. Promizole® was discontinued on account of slight anemia and leukopenia. Streptomycin was continued, the dose being increased to 1.0 Gm. a day. This treatment was continued for three weeks. On July 27 all evidences of activity had disappeared and vision had risen to 20/40.

CASE 13.—A white man aged 37 was first seen March 18, 1949. The family and past histories were noncontributory. Retinal hemorrhages had developed in the right eye in 1942, and vision had been reduced in this eye since that date. The left eye was first affected in February 1949. Examination showed bilateral retinal hemorrhages with secondary gliosis, and vision was reduced to 1/200 in the right eye and to 20/70 in the left eye. The medical survey, including biopsy of a lymph node, was noncontributory entirely except for violent hypersensitivity to tuberculin (0.001 mg.) and calcified hilar nodes on roent-

genologic examination. The patient was a veteran and was referred to the Veterans Hospital for streptomycin and promizole® therapy, which was started on April 19. He was given an extremely large dose of streptomycin, 2 Gm. twice daily and 6 Gm. of promizole® daily. Treatment was continued without toxic symptoms up to May 31. The total dose was 168 Gm. of streptomycin and 252 Gm. of promizole®. Examination on June 10, 1949 showed vision of 20/100 in the right eye and of 20/100 in the left eye. The hemorrhage had entirely disappeared. Without further treatment of any kind, the vision on July 12, 1949 was 20/100 in the right eye and 20/40 in the left eye. The right fundus showed a mass of glial tissue extending from the disk and involving the fovea. The left fundus showed a discrete mass of glial tissue between the disk and the fovea, with some secondary granular degeneration of the fovea. There were no hemorrhages in either fundus or any suggestion of activity.

CASE 14.—A Negro aged 31 was admitted to the hospital on June 2, 1949, with a history of loss of vision of three weeks' duration. The family and past histories were noncontributory. Examination revealed that vision was reduced to counting fingers in the right eye and to 20/50 in the left eye. The eyes appeared normal to external inspection and examination with slit lamp. Ophthalmoscopic examination showed retinal and vitreous hemorrhages in both eyes, with areas of retinitis proliferans and glial bands extending up into the vitreous. Evidently, the eyes had been the site of repeated hemorrhages for some time, despite the history of onset three weeks previously. The medical survey was entirely noncontributory except for pronounced hypersensitivity to tuberculin and roentgenographic evidence of an old thickened pleura at the base of the right lung. All blood studies gave normal results. Streptomycin and promizole® therapy was started on June 8 and continued for forty-two days, to July 20. There were repeated hemorrhages in the left eye for the first three weeks, and vision decreased from 20/50 to finger counting. Thereafter there were no fresh hemorrhages, and the vitreous cleared steadily in both eyes and the old retinal hemorrhages partially absorbed. On July 9 vision had improved to 12/200 in the right eye and 8/200 in the left eye. On his discharge on July 20, there was no evidence of any hemorrhage, and glial bands were unchanged. Vision had risen to 20/30 in the right eye and 6/200 in the left eye.

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## FUNDAMENTAL CONCEPTS IN GLAUCOMA

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THE CONVENTIONAL classification of primary glaucoma which has long been accepted involves a division of its clinical manifestations into two types—simple (or noncongestive) glaucoma and congestive glaucoma. As a general rule the first type develops slowly, quietly and insidiously over many years with a characteristic triad of symptoms—raised tension, typical field defects and cupping of the disk—until in the “absolute” stage the eye becomes intensely hard, all vision is lost and the disk develops a deep, atrophic cup. The second type, on the other hand, is generally characterized by episodic subacute attacks of raised tension, the most notable features of which are the diminution of vision and halos caused by corneal edema; from the less severe of these episodes the eye may seem to recover to a considerable extent, but subsequent attacks tend to involve a permanent raising of the tension (chronic congestive glaucoma) or an acute attack may abolish vision. It is to be noted that the differentiation between the two types is not based on tension, for an eye showing the picture of simple glaucoma may have a tension much higher than one with acute congestive glaucoma. The differentiation depends on the state of the circulation: In the congestive type the primary lesion—at any rate a primary association—is a capillary stasis with increased permeability leading to edema of the tissues of the eye, while in the simple type signs of uveal congestion and edema are absent. To these a third type is sometimes added, forming a subgroup of the simple type; this is characterized by typical glaucomatous changes in the visual fields and atrophic cupping of the disk but without raised tension.

At the meeting of the American Academy of Ophthalmology and Otolaryngology in 1948<sup>1</sup> this classification was “thrown out of the window” as “thoroughly outmoded.” In a symposium in which Derrick Vail, Jonas Friedenwald, Peter Kronfeld, Harold Scheie, John Dunnington and Paul Chandler participated, the classification of primary glaucoma into narrow-angled and wide-angled types, proposed by Raeder in 1923, was unanimously and enthusiastically adopted. It is obvious that a collection of opinion and experience so authoritative will

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1. Vail; Friedenwald; Kronfeld; Scheie; Dunnington, and Chandler: Symposium on Glaucoma, *Tr. Am. Acad. Ophth. & Otolaryng.* 53:169, 1948.

carry an immense amount of weight on both sides of the Atlantic. The purpose of this paper is to inquire whether the suggestion is based on philosophic principles and is an aid to our understanding of that heterogeneous collection of ocular ailments which are characterized by a rise in intraocular pressure or by the symptoms traditionally associated with such a rise.

To a large extent the two systems of classification run parallel. By and large, the cases of narrow-angled glaucoma are congestive in type with an episodic and cumulative clinical history; similarly, the wide-angled type includes most of the cases formerly classified as glaucoma simplex. Based on this single anatomic characteristic, treatment is said to follow in a routine way. In the narrow-angled type surgery is the primary indication—basal iridectomy in cases of acute glaucoma before peripheral anterior synechias develop, iridencleisis after; a filtering operation in cases of the more chronic form. In the wide-angled type operation is advised only when medical treatment has failed, as shown by persistence of a raised tension or a fall in the function of the eye, when a filtering operation should be performed. It would seem that everything depends on raised tension, and that the raised tension itself depends on the width of the angle of the anterior chamber. I wish it were so easy.

From the logical point of view, the matter resolves itself into an inquiry whether the width of the angle of the anterior chamber is in fact the determining factor in the incidence of glaucoma and in the clinical characteristics shown by any particular case. I do not think it is. The immediate (or local) cause of congestive glaucoma is edema of the globe due to uveal vascular congestion. As would be expected from the anatomic layout of the circulation, this congestion particularly affects the ciliary region, and the consequent swelling and edema push forward the root of the iris, narrowing the angle of the anterior chamber until the iris may touch the cornea. If such a condition is marked, and persists, an acute, strangulating attack of glaucoma may ensue; if the engorgement subsides, the swollen tissues may retract, perhaps leaving some peripheral synechias; but if the process is repeated, an ever-increasing number of synechias, depending mainly on the height and duration of the raised pressure, are formed during subsequent attacks, each of which reduces the margin of safety, a chronically raised tension results and the stage is set for a final strangulating attack. It is, of course, obvious that the narrower the angle of the anterior chamber, the sooner such a culmination will ensue; and if the angle is sufficiently wide no acute incident may happen. But the whole of the story is not contained in this apparent blockage of the angle, for, on the one hand, in some 20 per cent of cases of acute congestive glaucoma the angle is found to be open on gonioscopic examination and, on the other, in some cases aqueous humor can be

seen flowing out in the aqueous veins when to all appearances the angle is blocked—a circumstance which becomes more significant when we consider the therapeutic effect of operations designed to establish drainage. The important considerations are that the primary cause of the disease is vascular congestion, that the likelihood of the development of an acute crisis depends largely on the narrowness of the angle, that the synechias which may partially or completely close the angle are the result, not the cause, of the raised tension and that, even in their presence, the drainage of aqueous humor need not be completely suspended.

The effect of surgical treatment in those cases is instructive. Most surgeons are agreed that in the prodromal stage of primary congestive glaucoma a small peripheral iridectomy will usually serve as an efficient prophylactic measure against future attacks. It can hardly be argued that such an operation, leaving a firmly healed cicatrix, can be effective by opening up sufficient drainage channels to insure safety; the more likely explanation seems to be that local axon reflexes determining congestive attacks are in some way inhibited. Similarly, gonioscopic examination of basal iridectomies performed in acute or subacute cases of glaucoma shows that the operation is rarely truly basal. The root of the iris, and sometimes the ciliary processes, are frequently adherent to the corneal wall of the angle; yet in many cases in which the angle seems to have been opened up the tension remains raised, and in as many cases in which the angle remains demonstrably blocked the tension is reduced to normal. While a freely open outlet is undoubtedly a factor never to be despised, and is sometimes of crucial importance in preventing or controlling a future crisis, the effect of the operation is often explained more rationally by a modification of the circulation in the anterior uvea than by a mechanical reopening of wide channels for drainage. Moreover, after an iridencleisis the angle can be shown to have become closed, and a flattened scleroconjunctival scar disproves the persistence of drainage at this point, while the tension remains normal; or, again, after a trephine operation the presence of goniosynechias, or a prolapse of the iris root or the ciliary processes or a flattened, adherent conjunctival flap may be compatible with the maintenance of normal tension, observations suggesting that one factor in the rationale of the operation may be that the operative trauma to the anterior uvea has broken a vicious circle that has determined vascular congestion. In a similar way, the control of the inflammation, and therefore of the congestion, in a case of hypertensive uveitis may result in a reduction of the ocular tension even in the presence of total annular goniosynechias. In all these cases the primary lesion is the vascular congestion; the state or configuration of the angle of the anterior chamber is secondary; clinically, a similar acute crisis may develop with an open or a closed angle, and the tension may well be lowered in the

absence of drainage through the operative cicatrix or be maintained in its presence.

When we consider wide-angled glaucoma, the difficulties increase. Wide-angled glaucoma is not associated with any characteristic depth of chamber, and it may occur in the presence of a wide or a narrow angle; the fact that it would appear to have nothing to do with the dimensions of the anterior chamber or the state of its angle makes it somewhat illogical to define the disease in terms of the angle, but suggests a definition based on the absence of congestion, which is, after all, the essential difference from the other type. So far as my experience is concerned, the angle is normal or wide in about 60 per cent of such cases and narrow in some 40 per cent. Gonioscopy shows that peripheral synechias are rare (occurring in 10 to 15 per cent), discrete, late and incidental. They are, however, frequently seen as the result of postoperative collapse of the anterior chamber.

In the symposium<sup>1</sup> at Chicago, "glaucoma occurring without tension" was stated to be rare (Friedenwald). The relatively common cases of glaucoma which occur in the absence of demonstrably raised tension were said in general to be instances in which a rise in tension occurred intermittently or the height of the tension measured tonometrically was masked by scleral rigidity. With this I find it difficult to agree. I think there are a considerable number of cases characterized by typical glaucomatous cupping, which is frequently very deep and atrophic, and typical slowly progressive glaucomatous field defects but with long retention of the central field, so that, in the absence of complicating raised tension, the disease rarely, if ever, progresses to complete blindness, usually occurring binocularly, but sometimes unilaterally, in persons over 50, and often over 60, most frequently women with a relatively low blood pressure and a low dynamometric reading in the retinal artery—all these signs without any demonstrable rise of ocular tension as taken over periods of years. Sometimes no rise of tension can be demonstrated during periodic visits to the hospital, when several readings are taken each day, or in provocative tests. When the disease occurs unilaterally, the tension in the affected eye may be the same as that in the other, or even somewhat lower; but sometimes (and this, as we shall see, is important) after the lapse of many years the tension may eventually rise, in which case blindness may ensue.

This type of case brings up the importance of the nature and rationale of the cupping of the optic disk. The pathologic picture in such a disk is characterized by early disappearance of the nerve fibers without a reactive increase of glial or connective tissue, so that cavernous lacunas are formed. Such lacunas have been seen in the retina (Schnabel,<sup>2</sup>

2. Schnabel: *Arch. f. Augenh.* 24:273, 1892; *Ztschr. f. Augenh.* 14:1, 1905: 19:558, 1908.

Schreiber,<sup>3</sup> Redslob<sup>4</sup>) anterior to the lamina cribrosa, immediately behind it and far up the optic nerve (Behr<sup>5</sup>). A primary and constant accompaniment is vascular sclerosis with disappearance of the capillaries. The whole picture suggests that the changes are typical of what happens to a complex tissue when the blood supply is gradually cut off—the more highly differentiated elements degenerate and disappear without any attempt (owing to the lack of blood supply) at proliferation by the supporting tissues, which, in fact, themselves eventually break down, so that the original small cavities coalesce into large lacunas (Wolff<sup>6</sup>). It is possible that in some cases these vascular changes are secondary to pressure; it is equally possible that in others they are primary. The frequent resistance of the disk to long-standing high pressure in many cases, such as is seen typically with hypertensive iridocyclitis, as compared with the deep cupping so often seen in cases of chronic glaucoma with relatively little (or no) abnormal pressure, would seem to indicate that raised pressure alone is not the sole determinant of the condition. It is probable that the disappearance of the nerve tissue and the weakening of the supporting tissue at and around the lamina may allow the formation of a cup with a normal (or even a subnormal) intraocular pressure. Even in simple glaucoma the depth of the cup bears no constant relation to the tension of the eye.

A note is necessary on the association of cupping of the disks with atrophy and typical glaucomatous field defects sometimes seen in cases with calcified and dilated carotid arteries, a type of case particularly illuminated by Arnold Knapp.<sup>7</sup> Friedenwald accepted the suggestion of Thiel<sup>8</sup> that these changes are the result of pressure on the optic nerve by the calcified artery. The fact that pressure on the nerve by any of the many space-taking lesions that frequently occur in the chiasmal region (aneurysms, pituitary tumors, meningiomas) never produces such changes at the nerve head or in the fields, even though the pressure may eventually involve complete blindness, makes it much more likely that sclerosis of the small vessels of the nerve associated with the sclerosis of their feeding artery is the cause of the lesion, rather than lateral pressure alone.

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3. Schreiber: *Arch. f. Ophth.* **64**:237, 1906.

4. Redslob: *Ann. d'ocul.* **172**:1, 1935.

5. Behr: *Klin. Monatsbl. f. Augenh.* **52**:790, 1914; *Arch. f. Ophth.* **89**:265, 1915; **133**:227, 1937.

6. Wolff: *Tr. Ophth. Soc. United Kingdom* **68**:133, 1948.

7. Knapp, A.: Association of Sclerosis of the Cerebral Basal Vessels with Optic Atrophy and Cupping: Report of Ten Cases, *Arch. Ophth.* **8**:637 (Nov.) 1932; Course in Certain Cases of Atrophy of the Optic Nerve with Cupping and Low Tension, *ibid.* **23**:41 (Jan.) 1940.

8. Thiel: *Ber. ü d. Versamml. d. deutsch. ophth. Gesellsch.* **48**:133, 1930.

It would seem that in the simple type of glaucoma the factor determining the rise of tension is not the dimensions of the angle, but some subtler obstruction to the drainage of the aqueous humor. This is borne out by the recent evidence of gonioscopy that it is difficult to force blood back from the episcleral veins into Schlemm's canal in established cases of simple glaucoma even if the tension of the eye is normalized by operation or medical treatment. This reverse flow can usually be made to occur readily in the earlier years of life but is seen much more rarely (in less than 40 per cent of cases) in persons over 50 years of age. It would seem that some obstruction to the flow commonly tends to occur with age and that a similar blockage occurs in this type of glaucoma. What the cause of this obstruction in simple glaucoma may be is not known. It is not gonioscopically visible and presumably depends on sclerosis of the exit channels and the trabecular tissue, probably itself secondary to vascular sclerosis in this region; but it is quite clear that it has no relation to the width of the angle of the anterior chamber.

It would seem reasonable to assume that the fundamental pathologic processes occurring in the nerve head and at the angle of the anterior chamber are closely related, if not precisely similar. If the sclerosis affects both areas, there result a cupped disk and raised tension, giving the complete clinical picture of simple glaucoma; if the former alone, there is glaucoma without raised tension; if the latter, there is raised tension with cupping of the disk and field loss as a late and consecutive event. Finally, an increase in tension at a late stage in a case of the "posterior" type is readily explicable by the spread of sclerosis from the posterior to the anterior vessels of the eye. If a term is required to differentiate the occurrence of the process of sclerosis limited to the posterior segment of the eye, "sclerotic optic atrophy" may be found suitable in view of the fact that the connotation of the word "glaucoma" is bound up with the concept of increased tension.

A consideration of the results of treatment of this type of glaucoma is also of importance. Taking simple glaucoma as a whole, my experience shows—and I think it is a fair average—that of eyes in which operative treatment has been adequate and the tension has been brought under control, about 30 per cent do not do well; even of eyes in which the tension has been controlled early, some 15 per cent do badly, and of eyes in which the tension is controlled late, some 50 per cent deteriorate—all despite the persistent and adequate control of tension. It is my impression that if the disease were not one of old age, and patients had a longer average of life after the development of symptoms, this percentage would be considerably higher. I have studied particularly a series of 10 patients all with bilateral typical simple glau-



coma—some with a considerable degree of tension, others with little or none. When tension was present, each eye was trephined and the tension (apparently) normalized; nevertheless, the visual function slowly deteriorated. One eye in each case was subsequently subjected to several operations until the tension was maintained consistently at a subnormal level (about 10 mm. mercury Schiøtz); and in each case the deterioration of function in the two eyes continued to run on in parallel lines. There was no possibility of intermittent rises of tension in the eyes repeatedly operated on. I think the results of all the filtering operations—corneosclerotomy or iridencleisis, or any of their innumerable modifications—give practically identically comparable results; in all of them the tension may well be normalized even if gonioscopy shows the operative channel to be occluded or conjunctival filtration is completely absent. If the be-all and end-all of simple glaucoma were contained in the angle of the anterior chamber and the disease were merely a question of raised tension, there ought to be few functional tragedies in the experience of an enthusiastic surgeon.

Finally, the question of secondary glaucoma should be considered. By "primary" glaucoma we mean a glaucoma the ultimate cause of which is still unknown; by "secondary" glaucoma, those forms due to an established lesion; the former is a concept which will disappear in the future as our knowledge grows. The slit lamp enables us to see minute keratic precipitates, and in a large number of cases glaucoma hitherto known as primary becomes secondary. Senile exfoliation of the lens capsule is discovered, and another batch of cases enters the category of the "known"; Reese<sup>9</sup> described a dystrophic type in which Descemet's membrane and endothelium encroach on the angle of the anterior chamber, and the total of primary glaucomas is again diminished. Any classification of glaucoma should therefore logically include all types.

An issue of this journal dedicated to the life's work and genius of Arnold Knapp is a suitable medium in which I may be sufficiently conservative—or, alternatively, not sufficiently precipitate—to express a preference for the classic classification into *congestive* and *simple* (*noncongestive*) types on the grounds that it is philosophically valuable, since it suggests the fundamental nature of the disease, and is helpful in that it aids in the determination of treatment. Congestive glaucoma is primarily due to vascular imbalance involving congestion, stasis and edema. It may be caused by several factors which are known, such as inflammation, trauma, subluxation of the lens and venous obstruction (secondary glaucomas), or it may be due to vascular crises or instability, the ultimate cause or causes of which are not yet known but

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9. Reese, A. B.: Am. J. Ophth. 27:1193 (Nov.) 1944.

some of which we may surmise may depend on neurohumoral, endocrine, thalamic, psychosomatic or purely local factors (primary glaucoma). In all these cases narrowness of the angle is of importance, since it may bring about an acute crisis by strangulating the ocular circulation; but narrowness of the angle is not causal; it is merely an incident which may affect the course of the disease. Simple glaucoma, on the other hand, is not associated with the picture of vascular congestion. We are very much in the dark as to the cause, and, largely from lack of knowledge of the factors which determine the formation of the intraocular fluid, we have been led to concentrate mainly on the effects of hindrances to its absorption and drainage. Accepting this limitation, we can conclude that the change is mostly of the "anterior" type, acting presumably through obstruction of the drainage of the intraocular fluids (and thus involving raised tension). The obstruction may be due to known factors, such as persistent embryonic tissue (buphthalmos), a growth backward of Descemet's membrane and endothelium, a growth forward of cicatricial tissue from the iris (progressive atrophy of the iris), the deposition and organization of inflammatory material or the deposition of flakes from the lens capsule (secondary glaucomas), or to subtler changes the nature of which we do not yet know but which we suspect are generally of a sclerotic nature (primary simple glaucoma): it is possible that the same type of change confined to the posterior part of the eye may produce corresponding visual changes in the absence of raised tension (sclerotic optic atrophy). In none of these types of glaucoma does the condition of the angle matter, be it wide, normal or narrow. Any type of glaucoma may indeed occur with any type of angle.

I would not give the impression that a rise of tension is a matter of no importance: The reverse is the case, for in its continued presence any eye will probably go blind, and, what is of the highest practical importance, the control of tension is almost the only method of therapy available to us in view of our present ignorance of the ultimate cause of many cases of the disease or in view of our inability to influence some of the etiologic factors which we do know. But it is merely a complication—a complication, however, that must be watched with constant and anxious care, that on occasion may be all-important and catastrophic, or, alternatively, may be merely incidental or even non-existent—occurring in the course of at least two, and probably more, fundamental maladies. Nor would I decry the undoubted importance of the width of the angle in certain cases, but it is merely an anatomic peculiarity which sometimes influences the gravity of this complication. It seems to me that to make it the central pivot around which the subject of glaucoma hinges is a suggestion lacking in philosophy and full of practical pitfalls.

## SARCOIDOSIS INVOLVING THE ORBIT

### Report of Two Cases

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ROCHESTER, MINN.

SOME pathologists believe that sarcoidosis is a type of noncaseating tuberculosis, while others maintain that it is a separate disease entity of unknown origin. The similarity of the clinical manifestations of sarcoidosis and tuberculosis and the resemblance of the biopsy findings frequently make the differential diagnosis of these diseases difficult. In cases in which the presence of acid-fast bacilli can be demonstrated, there is no question about the diagnosis; but in the absence of clinical signs of tuberculosis and in cases in which examination fails to disclose *Mycobacterium tuberculosis*, the biopsy findings may be considered characteristic of either tuberculosis or sarcoidosis.

I shall report 2 cases of sarcoidosis of the orbit which have been observed at the Mayo Clinic.

### REPORT OF CASES

CASE 1.—A white woman aged 54, a native of Puerto Rico, came to the Mayo Clinic on Jan. 21, 1926 because of a mass in the left orbit, which she had first noticed in November 1925. The initial symptom had been pain about the left orbit and on the left side of the head. The pain had extended to the left shoulder. Within a few weeks the upper lid had dropped, and she subsequently had been unable to open the left eye. Her previous general condition had been entirely satisfactory.

Vision was 6/7 in the right eye and 6/20 in the left eye. The right eye was normal in appearance, and its functions were unimpaired. In the left orbit a mass could be felt beneath the upper margin. It extended from the area of the supra-orbital notch to the temporal rim and along the lower margin to the infraorbital notch. The anterior edge of the tumor, as it appeared on palpation under the orbital rim, was sharp, movable and flexible, but firm. The mass was attached to the temporal border of the orbit. There was moderate chemosis of the lateral half of the globe. The cornea was clear, and the anterior chamber was shallow. The pupil was D shaped, with the curved portion directed temporally. Exophthalmometric readings were 20 mm. for the right eye and 19 mm. for the left eye. Ophthalmoscopic examination did not disclose any abnormality of either eye. Roentgenograms of the orbit were normal. A diagnosis of orbital tumor was made, and operation for its removal was performed on Jan. 27, 1926. The tumor was firm and extended from the region of the supraorbital notch around the temporal wall of the orbit and in the lower lid to the infraorbital notch. It was

removed by blunt dissection. The mass extended into the lower eyelid beneath the skin (fig. 1). It was firmly attached to the skin of the lower lid. The tumor was 1 cm. thick and had a scanty blood supply. It was not encapsulated but was surrounded by loose areolar tissue. Removal of the tumor caused a slight hemorrhage. The external rectus muscle and the lacrimal gland had to be removed with the tumor. The pathologic diagnosis was tuberculosis. The patient was dismissed from the clinic on Feb. 24, 1926.

On Feb. 19, 1948, I examined the patient in San Juan, Puerto Rico. The patient was well, and she had not observed any evidence of recurrence of the tumor. Her family physician said that the patient had never shown any evidence of tuberculosis elsewhere than in the orbit.

Original sections of the tumor were reexamined twenty-three years after its removal, and additional sections were cut and examined microscopically. The histologic picture was that of noncaseating tuberculosis, or sarcoidosis. The sections contained numerous tubercles, or nodules, of epithelioid cells associated with a considerable number of multinucleated giant cells and surrounded by a rather scanty infiltration of lymphocytes and plasma cells. A few small areas of degeneration were seen. The tubercles were packed closely in the tissues of the orbit. The lacrimal gland also was involved by the tumor. The involved portion of the lacrimal gland contained fewer nodules of epithelioid cells and a denser infiltration of lymphocytes than the involved portion of the orbit.

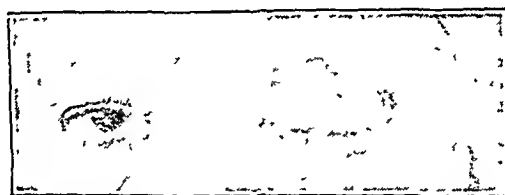


Fig. 1 (case 1).—Tumor of the left orbit involving the lower eyelid.

CASE 2.—A white woman aged 72, a native of a midwestern state, came to the clinic on Nov. 23, 1948. In August 1948 she had noted a foreign body sensation in her right eye. A short time later the upper lid of the right eye had become swollen. The swelling of the lid had increased gradually, without inflammation or pain. In August 1948 a mass had appeared in the superior temporal quadrant of the right orbit. The mass had increased in size and had caused some exophthalmos and swelling of the lower lid.

Visual acuity, with correction, was 20/30 in each eye. A palpable mass was present in the anterior portion of the right orbit and involved the upper and lower eyelids. It extended deep in the superior temporal quadrant of the orbit. Rotation of the eye was only slightly impaired. On the temporal side, the mass was continuous from the supraorbital notch to the infraorbital notch. Readings obtained with the Hertel exophthalmometer were 17 mm. for the right eye and 15 mm. for the left eye. External examination of the right eye did not disclose any abnormality. The media were clear, and the ocular fundus was normal. The concentration of total protein was 6.1 Gm. per hundred cubic centimeters of serum; the values for the albumin and globulin were 4.2 and 2.0 Gm., respectively, per hundred cubic centimeters of serum. The reaction to the Kline test of the serum was negative. The preoperative diagnosis was orbital tumor, probably adenocarcinoma (fig. 2).

On Dec. 3, 1948 the tumor was removed completely except for a small portion which was situated in the lower eyelid near the external canthus. It was necessary

to remove portions of the levator palpebrae superioris, superior rectus and external rectus muscles which were enmeshed in the tumor. The mass extended into the orbit for a distance of 3 cm. Grossly, it appeared pale and granular.



Fig. 2 (case 2).—Tumor of the right orbit involving the lower eyelid.



Fig. 3.—Section ( $\times 75$ ) of the mass removed in case 1 in 1926. The diagnosis was tuberculosis. On reexamination in 1948 the resemblance to sarcoidosis was noted.

Microscopic examination revealed that the tumor was composed of many small tubercles, or nodules, consisting of groups or whorls of epithelioid cells, surrounded by fibrous tissue. Fairly numerous large multinucleated giant cells were seen,

chiefly at the periphery of the nodules, although in some of the nodules there was a solitary giant cell at the center. A scanty mantle of lymphocytes surrounded many of the nodules, and occasionally there was a scattering of lymphocytes at the center, sometimes associated with a very small, degenerated-appearing area, but with no evidence of caseation. Many of the larger nodules were irregular in shape and appeared to be conglomerations of smaller nodules. The nodules were invading, and in large part replacing, orbital connective and adipose tissues in the involved area, and to a lesser extent were invading the lacrimal gland. In the lacrimal gland and in other areas near the periphery of the lesion, the lymphocytes appeared relatively more numerous and the nodules of epithelioid cells smaller and scantier. The diagnosis was sarcoidosis (figs. 3 and 4).



Fig. 4.—Section ( $\times 75$ ) of the mass removed in case 2, in 1948. The diagnosis was sarcoidosis.

After the pathologic diagnosis of sarcoidosis was made, the patient was reexamined for other evidence of the disease, but none was found. She was dismissed from the clinic on December 18.

On Feb. 3, 1949, the patient returned to the clinic because of a recurrence of the tumor in the right lower eyelid. The mass was excised from between the skin and the tarsal plate. A small portion of the skin of the eyelid was involved and had to be removed with the tumor. Bacteriologic examination of the tumor, including the making of cultures, examination of smears and subcutaneous and intraperitoneal inoculation of guinea pigs, did not disclose *Myco. tuberculosis*. Cultures also failed to disclose *Brucella* or fungi.

## COMMENT

This report is based on 2 cases of sarcoidosis of the orbit which were observed at the clinic in a period of approximately twenty-three years. These 2 cases represent the only instances of sarcoidosis encountered in more than 1,000 cases of tumor of the orbit observed at the clinic. Other cases in which sarcoidosis has been limited to the orbit probably have been reported in the literature, but I have not searched the literature for them. We know that tuberculoma of the orbit is rare. Unless case 1 is considered as a case of tuberculoma, not a single instance of tuberculoma of the orbit has been observed at the clinic. Orbital complications have not occurred in any of the other cases of sarcoidosis which have been observed at the clinic, but intraocular manifestations, such as iritis, chorioretinitis and uveitis, have frequently been present.

The condition known as sarcoidosis is characterized histologically by the presence of a granulomatous, tuberculosis-like lesion which contains epithelioid and multinucleated giant cells but is not associated with caseation necrosis. Some investigators believe that sarcoidosis is a separate disease entity of unknown origin, while others believe that it is a form of noncaseating tuberculosis. Those who believe that it is a separate disease entity usually make the diagnosis by a process of elimination. In cases in which a pathogenic form of *Myco. tuberculosis* is present, there is no question about the diagnosis of tuberculosis. A diagnosis of sarcoidosis is made in cases in which animal inoculation, bacterial culture and other tests fail to disclose any etiologic agent.

In both the present cases the tumor protruded from the orbital rim within four months after its onset. Both the patients were women who were past middle age. The history was not suggestive of tuberculosis in either case, and laboratory tests in 1 case likewise failed to disclose *Myco. tuberculosis*. No other sign of tuberculosis or sarcoidosis was found elsewhere in the body in either case.

The gross appearance of the two tumors was similar. Each tumor involved the eyelid beneath the skin. The involvement of the skin was so extensive that the tumor could not be separated. There was no history or sign of external injury which would account for the development of the tumor. The blood supply of the tumors was scanty. The growths were not encapsulated, but they could be separated from the contiguous tissue by blunt dissection.

In case 1, examination did not disclose any evidence of recurrence of the tumor twenty-two years after its removal.

Clinically, the orbital masses in these 2 cases were classified as tumors, although it is not our intention to place them in the category of neoplasms.

The Mayo Clinic.

# INVESTIGATION OF VISUAL SPACE

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SINCE January 1948 the chief problem for investigation by the staff of the Knapp Laboratory for Physiological Optics<sup>1</sup> has been the bases on which space perception and spatial orientation are founded. The work is grounded on Luneburg's "Mathematical Analysis of Binocular Vision,"<sup>2</sup> which incorporates new and important concepts regarding the fundamentals of space perception, which yields logical and accurate explanations of work already done and facts already known and which promises new possibilities in the experimental and clinical field of vision, with important predictive powers in the fields of art, architecture, industry and war.

## THE PROBLEM

Our problem is to discover, evaluate and mathematically express the fundamental, basic relationships between visual stimuli and the sensation they arouse, to find and verify the constant factors operating in this relationship and to seek and describe the underlying constant relationships between binocular stimulus and resultant sensation on which all the subsequent psychologic and experiential factors are added. Psychologically expressed, we are searching for a psychometric coordination. Mathematically expressed, the problem is to find, formulate and, in particular, to verify experimentally a coordination of the sensed points of a visual sensation with the points of a geometric manifold such that the apparent distance of any two sensed points is always proportional to the geometric distance of the correlated points.<sup>3</sup>

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This research is being conducted under contract N6onr-27119; project designation no. NR143 638. USN-ONR.

From the Knapp Memorial Laboratories for Physiological Optics, Institute of Ophthalmology, Columbia University College of Physicians and Surgeons.

1. In addition to the author, those working on this project are Dr. Rudolf Luneburg, mathematical consultant; Dr. Paul Boeder, mathematical consultant; Dr. Gertrude Rand, and Miss Catherine Rittler. Since September 1948 Dr. Anna Stein has served as full-time mathematical analyst. Mr. Arnold Kolodny has supplied mechanical assistance.

2. Luneburg, R.: *Mathematical Analysis of Binocular Vision*, Princeton, N. J., Princeton University Press, 1947.

3. Luneburg,<sup>2</sup> p. 1.



## ASSUMPTIONS

The problem is approached by making certain assumptions; checking these assumptions with observation, experimental validation and predictive value and from the mathematical and experimental data thus derived formulating further empiric steps. In such an approach, theory is constantly being modified and redirected by practice, and conversely, the direction and extent of experimentation are daily being changed by the implications of improved or extended theory. Despite ceaseless vigilance, unconscious assumptions (the results of our naïveté, our previous experience, teaching and bias) are likely to enter into our formulation.

The assumption consciously made is that there exists a relationship between physical stimuli and binocular sensation. If we do not accept this, the problem has no meaning. Since we are well aware of the fact that this relationship is not in one-to-one correspondence; that is, the qualities of visual sensation are not uniquely determined by the physical stimuli (the same physical stimulus can arouse different sensations and, conversely, different stimuli can arouse the same sensation), we are forced to conclude that only certain special elements of visual sensation are determined by the stimuli. The essence of the Luneburg theory is that "there exist immutable relationships but that they are confined to the assignments of apparent size to physical line elements."<sup>4</sup> These are the relationships we want to know. They have been formulated mathematically and found to be in perfect agreement with the results of investigations by Helmholtz, Hillebrand, Blumenfeld, Fechner and Ames.

The assumption can be formulated thus: ". . . that the sensations allow recognition of greater and smaller, and of greater and smaller contrast"<sup>5</sup>; that is, that we may compare the sizes of two arbitrary line elements in space even if these line elements are not attached to the same base point. In effect, it presupposes the ability of the observer to make (usually almost instantaneously) a judgment of "greater or smaller and of greater or smaller contrast."

## DISCUSSION OF THE PROBLEM

Our visual sense dominates most of our life. Through vision, and particularly through the sensory perceptions aroused by three dimensional binocular vision, our relations to the external world are largely controlled. No other senses reveal nature and the world we live in with such clarity and directness. Color, brightness, form and localization are immediately and vividly sensed through our ocular apparatus. Through our eyes a direct relationship to nature seems to be established.

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4. Luneburg,<sup>2</sup> p. 4.

5. Luneburg,<sup>2</sup> p. 6.

That there is a relationship between our visual sensations and the world we live in is assumed as obvious. But how direct is this relationship; how uniform is it, how does it vary in quantitative and qualitative terms; how can it be measured and expressed? These are questions as yet largely unanswered.

"Color," "brightness," "tone" are experienced and thought of as sensations, not as wavelengths, foot lamberts or relative reflectances. They exist in the brain as relative terms, and we know that some persons experience the same stimuli quite differently from others, even though they may be classified as normal observers. "Space," "form," "size," "distance"—these are now included in this category of perceptions which exist in the brain—in our experience—only.

Our sensations are not in one-to-one relationship with the physical counterpart. One unit of physical measurement does not cause 1 unit of perception. Only certain special elements of visual sensation are determined by the stimuli. The brain (perception) adds to a stimulus meaning, significance. Our "sensed" world and the physical world may be similar or not—certainly they are different. How can we show this?

In order to do so, we must differentiate between sensed or "visual space" and "physical space." These two have often been naïvely identified, but this misconception is not permissible.

1. "Physical space" is the measured mappable, blueprint space of the outside world. It is the space in which houses, railroads, bridges and streets are mapped and constructed with great precision. In measuring this space (within small tolerances), all engineers will come out with the same answer. Can we make such measurements in visual space?

2. "Visual space" is the immediate, instantaneous impression we have of our environment as a three dimensional manifold. We have an immediate sensation or impression of objects about us in relative terms: farther, nearer; larger, smaller or equal.

The question immediately arises: What is the relationship between these two spaces, physical space and visual space? Can we find a coordination between the sensed points in visual space and the correlated points in some geometric space such that the apparent distance of any two sensed points is always proportional to the geometric distance of the correlated points?

The entrenched misconception of the identity of the two spaces is the basis of the projection theory of spatial localization, which asserts that a point is sensed at the intersection of the two visual lines. Although useful in some respects, it can be reduced *ad absurdum* on the first attack; e. g., we know that railway tracks, although parallel physically, appear to converge in the distance. This problem has engaged critical minds for

centuries. The physical size of the moon cannot be sensed. A star's distance cannot be sensed. The sky appears not as an infinite space but as a finite, curved dome. These facts break down the projection theory.

On the other hand, the size of the retinal image does not explain these phenomena, because if this were so we would see like a camera, which always shows mountains too small. A man walking away from us retains his apparent size, although the retinal image grows rapidly smaller. This phenomenon is known as "size constancy" in the visual space. It is strongest in our own immediate vicinity. It fails and gradually collapses beyond about 100 meters, the distance depending on the observer.

#### IMPORTANCE OF THE PROBLEM

The problem is of much more than academic interest. As already noted, it is of potentially great importance in the fields of art, architecture, industry and war. If the metric (the rule, the formula, the measuring rod) of visual space can be formulated, one of the oldest and most interesting problems, the sensory perception of three dimensions by binocular vision will have received considerable clarification. Historically, this would be a great step forward in visual physiology.

In art and architecture, once the metric of visual space is known, the laws of pictorial reproduction can be derived without great difficulty. This would give us a theory of visual perspective quite different from the perspective based on projection from one center. Most certainly, the older technics of vanishing point and central projections would be greatly modified or discarded.

In ophthalmology, knowledge of this metric would yield new insight into all the problems of monocular versus binocular vision; of single binocular vision, fusion, heterophorias and heterotropias; of suppression, stereopsis, ametropia and aniseikonia.

In industry, aside from the architectural implications, one would expect to find important characteristics of groups as a whole (related to plant structure, layouts, stereoscopic representation, safety controls, motion picture technics), as well as of individuals (crane and machine operators, motor drivers, aviators, clerical workers) on which to base plans and selections.

In military and naval practice, a knowledge of the metric of visual space and of the constants characterizing a person in his perception of, and orientation to, objects in physical space would be of great value in the selection and training of personnel. It is for this reason that these investigations at the Knapp Laboratory have for the past year been under the sponsorship and support of the Office of Naval Research.

Every increase in speed of human-controlled carriers calls for a corresponding quickness of orientation and adjustment, and any contribution to the understanding of individual skills and abilities in this field is of great importance. In stereoscopic optical instruments, such as microscopes and range finders, a situation of clueless vision is realized to a considerable degree.

The purpose of these instruments is to determine the physical shape and localization of unknown objects by their apparent shape and localization in a visual space. It is clear that the results can be trusted only if the relation of visual binocular perception to the physical reality is quantitatively known.<sup>6</sup>

#### BACKGROUND OF THE PROBLEM

Many serious and careful investigations have been made to determine the differences and the relationships between the two spaces "physical" and "visual." I shall here mention only a few of the most important.

1. Helmholtz<sup>7</sup> observed, as before him others had observed, that what seemed to be straight in the horizontal frontal plane was not physically straight. A simple and quickly performed experiment will permit anyone to verify this statement for himself: If, in a darkened room, at eye level, and at about 1 to 2 meters distance, five or more small, dim lights (resembling stars) are arranged in what appears to be a perfectly straight line lying in the frontal plane, this line, when viewed from above, will be found to be not physically straight but markedly curved toward the observer. The amount of curvature will depend on the distance from the observer, the nature of the test objects used and the individual constants or characteristics of the observer. However, for all so-called normal binocular observers, under a given set of experimental conditions (same test objects, same procedures), there will be a range of distances in which the physical curvature is toward the observer (the shorter the distance, the greater the curve); a distance (or narrow range of distances) at which, for a line subtending an angle of 20 to 40 degrees, the apparently straight line is physically straight, and, beyond this, a distance at which the apparently straight line is physically convex toward the observer. (With more fun, equal interest and less bother, a similar experiment can be performed in broad daylight. With the subject squatting or lying so that the eyes are near ground level, an assistant arranges five golf balls on a relatively flat lawn or green 20 to 40 feet [6 to 12 meters] away. The balls are to

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6. Luneburg, R.: *Metric Methods in Binocular Visual Perception Studies and Essays*, Courant Anniversary Volume, New York, Interscience Publishers, Inc. 1948, pp. 215-240.

7. Helmholtz, H.: *Physiological Optics*, Optical Society of America, 1925, vol. 3, p. 318.

be arranged so that they appear to lie in a perfectly straight line at right angles to the line of sight. At this distance the physical curve will probably be convex toward the observer.)

This astonishing fact—that what is visually straight is not physically straight—has been recorded and confirmed many times but has never been explained in terms of basic principles, not even by Helmholtz.

2. These observations led Helmholtz and others to continuations of the experiment. In particular, Hillebrand<sup>8</sup> extended the Helmholtz observations on the frontal plane to walls at right angles to these horopters. The experiments are a little more complicated but just as dramatic and conclusive in their results.

Hillebrand showed that if the test objects (such as vertical strings or wires) were arranged in what appeared to be two perfectly straight and parallel lines (like the walls of an alley), such lines were physically neither straight nor parallel. The curvature changed both with the distance from the observer and with the individual observer (and probably with the type of test object and experimental procedure). Despite these variables, a basic pattern was demonstrable, reproducible and incontrovertible.

3. Blumenfeld<sup>9</sup> repeated, extended and greatly refined Hillebrand's experiment and added an amazing and interesting fact to the store of knowledge already accumulated. Using the same materials, procedures and observers and modifying only one factor in the situation, he produced two different curves which, according to his reports, were consistently and reliably reproducible. Leaving the farthest pair of test objects in exactly the same position, Blumenfeld required his observers, first, to set the other pairs of test objects so that the visual sensation was one of "equidistance"; that is, to the observer the distance between any pair of test objects appeared to be exactly the same as the distance between any other pair—the walls of the alley were "equidistant." These findings having been recorded, the experiment was repeated with nothing changed except the instructions to the observer: The observer was now told to set the test objects so that they would form two straight "parallel" lines, the visual criterion being that of "straightness" and "parallelism"; i. e., no matter how far forward or backward the "straight" walls were projected they would not meet. The "equidistant" and "parallel" curves were not the same. This is a paradox—inexplicable in Euclidean geometry because in Euclidean geometry parallel lines are equidistant. "Equi-

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8. Hillebrand, F.: *Theorie der scheinbaren Grösse bei binocularem Sehen*, Denkschriften der mathematisch-natur-wissenschaftlichen Classe der Kaiserlichen Akademie der Wissenschaften, Vienna, 1902, vol. 72, pp. 255-307.

9. Blumenfeld, W.: *Untersuchungen über die scheinbare Grösse im Sehraum*, Ztschr. f. Psychol. u. Physiol. d. Sinnesorg. 65:241-416, 1913.

distant" and "parallel" mean the same thing. This paradox is another hint of different laws operating in the visual space. It is the first clue to the non-Euclidean<sup>10</sup> nature of the visual space.

4. Ames, who studied visual spaces, found other differences between "visual" and "physical" space. His demonstrations of "equivalent configurations" are important and valuable contributions to our growing knowledge of visual space. "Equivalent configurations" supply beautiful and irrefutable evidence that different configurations of physical stimuli can give rise to the same visual sensation. Ames's "distorted rooms" is a superlative example of the difference between "physical" and "visual" space. These rooms are not perspectiveally related. They have become one of the foundations of a whole new theory of psychology, "perceptionism".<sup>11</sup>

These important basic facts must be considered in any theory of binocular vision or space perception. They can be neither overridden nor dislodged. They militate strongly against utilizing the Euclidean metric in visual space. But they lead also to new and important considerations regarding these two spaces, since, now being freed of the necessity or inclination to consider them as identical, we can inquire separately into the nature of each. This has led to the hope that our problem may be solved and that the relationship of the two spaces can be clarified.

The nature of physical space has been investigated for centuries. Whatever its shortcomings in distances approaching infinity, the Euclidean description of physical space is almost surely adequate in the range wherein human stereopsis functions.

Visual space is demonstrably not Euclidean in its nature. This being so, the question arises: Is there another metric geometry into which we may try to fit the known facts? There are two: the hyperbolic geometry of Bolyai and Lobatschewsky and the elliptic geometry. There are many other non-Euclidean geometries, but only these two maintain the necessary properties of constant curvature, of isotropism and homogeneity. An analytic study of these not only should give valuable information as to which most closely fits observed facts but should yield predictions for further useful experiments.

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10. Non-Euclidean is a term used by Gauss to describe a system of geometry different from Euclid's in that the Fifth Postulate regarding parallelism was not used. About 1820, Bolyai, in Hungary, and Lobatschewsky, in Russia, had each developed a non-Euclidean system. Later, Riemann, in Germany, and Cayley, in England, developed another system differing radically from Euclid's. In 1871 Klein classified the various systems, giving the name "parabolic" to the system developed by Euclid, "hyperbolic" to the system developed by Bolyai and Lobatschewsky and "elliptic" to the system of Riemann and Cayley.

11. Cantrill, H.: *Understanding Man's Social Behavior: Preliminary Notes*, Princeton, N. J., Office of Public Opinion Research, 1947, vol. 7, p. 75.

When the problem is attacked from the other end, important theoretic questions demand attention :

1. Is it possible to find a relationship between the two spaces so that we can go from one to the other?
2. Is it possible to find a coordination between two points in space and the sensation they cause?
3. Is it possible for us to predict what distance sensation will be aroused by two points in physical space?

This task has been attempted by Rudolf Luneburg, who has mathematically analyzed binocular vision with respect to size and distance sensation and has derived the "metric of the visual space"; that is, he has given a means by which we can measure in the visual space. This is, if verified, an important contribution.

What is a "metric"? It is a rule, a ruler, a measuring device, a formula, an equation for measuring distance in a given space. It will vary with different spaces; or, stated more significantly, if the metric is known, all the geometric characteristics of the space are known.

For example, for line geometry the metric is

$$ds \text{ (the line element, measured in any units)}$$

for plane geometry the metric is

$$ds^2 = dx^2 + dy^2 \text{ (the Pythagorean theorem)}$$

for solid geometry the metric is

$$ds^2 = dx^2 + dy^2 + dz^2 \text{ (plane geometry extended to three dimensions)}$$

for spherical trigonometry the metric is

$$ds^2 = d\phi^2 + \cos^2\phi d\theta^2 \text{ (The geodesic, shortest distance between two points, is the arc of a great circle.)}$$

A more general metric for three important geometries may be written as:

$$ds^2 = \frac{dx^2 + dy^2 + dz^2}{[1 + \frac{1}{4}K(x^2 + y^2 + z^2)]^2}$$

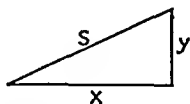
It is immediately apparent that if  $K$  (the Riemannian curvature of the space) is equal to 0, the denominator of this equation cancels out and we have the metric given for Euclidean geometry, namely,  $ds^2 = dx^2 + dy^2 + dz^2$ . In general, this formula fits all three geometries under the following conditions:

- If  $K > 0$  (elliptic metric)
- If  $K = 0$  (Euclidean metric)
- If  $K < 0$  (hyperbolic metric)

The last appears to be the metric of the visual space.

In Euclidean plane geometry, which we have all studied, the metric is

$$ds^2 = dx^2 + dy^2$$



That is  $ds$  is the distance to be measured, in any units, between two adjacent points. This metric is the very foundation of plane geometry.

Once we have it, we can derive any theorem—in fact, the whole structure of the geometry. It is the code script of the geometry; just as the gene holds the code script of the man. The whole structure and character of the geometry is determined by the metric; just as the whole structure and character of the man is determined by the gene.

The metric of the visual space is probably non-Euclidean, as was hinted in the discussion of the paradox of Blumenfeld's alley experiment.

We are all familiar with one type of non-Euclidean geometry because we are living on a sphere and two dimensional spherical geometry is non-Euclidean, that is, elliptic. That the spherical geometry is essentially different from the geometry of the Euclidean plane is shown by the fact that it is impossible to make a plane map of the earth without distorting distances. Still, it is possible to study the geometry of the earth with the aid of plane maps if the principle of construction of the maps, that is, the formulas for the distance between any two points, is known. Similarly, the geometry of the visual space can be studied if its "psychometric" is known. Here is the essence of Luneburg's contribution.

The psychometric of the visual space can be expressed, using appropriate binocular coordinates, in the following form:

$$ds^2 = \frac{4}{(e^{\sigma\gamma} + Ke^{-\sigma\gamma})^2} (\sigma^2 d\gamma^2 + d\phi^2 + \cos^2 \phi d\theta^2)$$

where  $K$  indicates the constant Riemannian curvature of the visual space. This formula establishes a relation between the visual and the physical space. It expresses the general hypothesis that, for an individual observer, the apparent size,  $ds$ , of a line element is uniquely determined by its physical coordinates  $\gamma$ ,  $\phi$ ,  $\theta$  and by two personal constants  $\sigma$  and  $K$ . According to this formula, judgment of visual size is based not only on the angular differentials  $d\gamma$ ,  $d\phi$ ,  $d\theta$  but also on the localization,  $\gamma$ , of the line element. The angular differentials  $d\gamma$ ,  $d\phi$ ,  $d\theta$  are related to

the size of the retinal image. In addition, the factor  $\frac{4}{(e^{\sigma\gamma} + Ke^{-\sigma\gamma})^2}$

is related to the sensed size. Our sensed scale of size seems to contract with increasing values of  $\gamma$ , namely, proportionately to the expression

$$\frac{4}{(e^{\sigma\gamma} + Ke^{-\sigma\gamma})^2}. \text{ Such a well defined contraction can probably be}$$

understood only if there is a physiologic basis for it, in the dioptric system of the eyes, on the retina, in the transmission to the brain or in the cortex itself. Luneburg makes no hypothesis concerning this.



That the metric of the visual space is dependent on personal constants is as it should be, for it is suspected that the visual space is different for different persons, and even for the same person at different periods of his life. It is probable that the values of these constants are related to the technical abilities, visual skills and the ametropia of the individual observer.

Luneburg has indicated that there are at least two such personal constants,  $\sigma$  and  $K$ , which should be determinable experimentally and which should yield a description of the sensed space of the observer. The constant  $\sigma$  (it may be a function of  $\gamma$ ), relates the sensitivity of depth perception to the perception of lateral size, and thus must be related to the interpupillary distance of the observer. Since the threshold of depth perception is considerably smaller than the threshold of size,  $\sigma$  will be considerably greater than 1. The constant  $K$  determines the geometric character of the visual space and thus must be considered as a psychologically significant constant which is characteristic for an individual observer. It is of importance for the relation of sensory judgment of size to physical size. Though the two will never be identical, one finds that the best approximation to physical size by sensory estimation is represented by the case  $K = -1$ . Indeed, in this limiting case, infinite distances are possible in the visual space. Thus, we conclude that the estimation of visual size of an observer agrees with the physical size the nearer to  $-1$  the constant  $K$  is found. It is quite possible that a correlation of mechanical abilities to the values of  $K$  can be established.

#### THE THEORY

The theory, then, is that visual space differs from physical space; that if the latter is Euclidean in our vicinity the former is certainly not; that the metric of visual space closely corresponds to, or is identical with, the metric of Lobatschewsky's hyperbolic geometry; that at least two, and probably more, personal constants enter into this metric; that these constants (like refractive errors, aniseikonia, stereopsis, etc.) are fairly stable for a given individual but may be modified by such factors as age, correction of refraction, experience and other factors; that they are probably also closely related to his mechanical and artistic skills, and that they may eventually prove to have considerable predictive value in regard to personnel selection for special tasks.

For devising experiments from the results of which the personal constants  $\sigma$  and  $K$  can be determined, there are certain elementary spatial judgments which can be utilized: (1) judgments of relative size and distance; (2) straightness of line, e. g., in a frontal plane or perpendicular to a frontal plane; (3) estimation of right angles or perpendicularity.

A mathematical analysis of the problems and paradoxes previously noted will lead to suggested procedures for determining the values of  $\sigma$  and  $K$  for different subjects, as well as indicating whether (as is probable) other constants are involved and what their relative values and importances are. Preliminary work has been carried out in this laboratory on several such procedures, utilizing a comparison of parallel and equidistant alleys, an analysis of certain phenomena observed on Vieth-Mueller circles, quantitative analysis of apparently straight lines in the horizontal plane perpendicular to the median line, the measurements of what appear to be right angles and studies of middistance spaces using plane mirror haploscopes.

It is important to emphasize that this study is merely an approach to the problem of visual space. It is not to be hoped that in a short time all the problems of space perception—including all visual phenomena—will be clarified and solved. It is equally important to note that the approach is new, logical, rational and promising. While I emphatically disclaim any competence to judge the mathematical soundness of Luneburg's derivations, I have taken pains to have them scrutinized by mathematicians of high standing and am assured of their validity. How we apply them, and with what success, lies in the realm of tomorrow.

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# SUBCHOROIDAL EXPULSIVE HEMORRHAGE OCCURRING DURING THIOPENTAL SODIUM (SODIUM PENTOTHAL®) ANESTHESIA

Its Treatment by Sclerotomy

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CHICAGO

EVERY ophthalmic surgeon, unfortunately, will experience, sooner or later, the occurrence of an expulsive hemorrhage in one or more of his patients after intraocular operation. It is a disastrous complication which probably cannot be foreseen, and for which there is little to be done when it does occur. The one form of treatment that has offered any hope of saving the eyeball at least is prompt incision of the sclera in the area of the hemorrhage and evacuation of the blood.

Posterior sclerotomy for this condition was first performed in 1915 by Verhoeff.<sup>1</sup>

His patient, a man aged 60, had bilateral chronic noninflammatory glaucoma. An iridectomy was performed on the right eye. Almost immediately thereafter vitreous began to pour from the wound. The eye became hard, and there was severe pain. Four hours later Verhoeff performed a sclerotomy to relieve the glaucoma. The first puncture with a Graefe knife was made on the nasal side of the globe, and only a small amount of blood escaped. A second puncture was made on the temporal side, and from this a large quantity of blood flowed and the eye partly collapsed. A third puncture was then made below the second, with the same result. The procedure was then regarded as useless, and the patient was returned to his bed.

During the night of the following day the pain became severer and a considerable amount of blood flowed from the eye, so that the bandage needed changing. From then on, however, uneventful healing occurred, and three weeks after the operation the vision was 20/200.

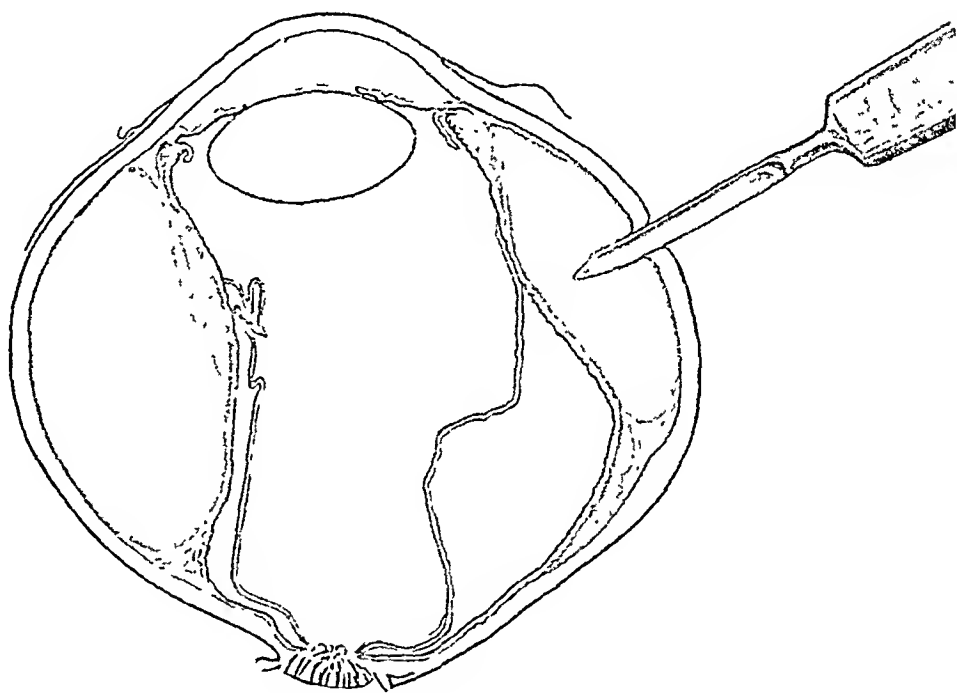
In 1937 I reported 2 additional cases in which the eyes were saved and some vision was maintained after posterior sclerotomy for expulsive hemorrhage. The first of these hemorrhages followed cataract extraction; the other followed an iridectomy for glaucoma. The details of these cases will be found in the report.<sup>2</sup>

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1. Verhoeff, F. H.: Scleral Puncture for Expulsive Sub-Choroidal Hemorrhage Following Sclerostomy, *Ophth. Rec.* **24**:55, 1915.

2. Vail, D.: Posterior Sclerotomy as a Form of Treatment in Subchoroidal Expulsive Hemorrhage, *Tr. Am. Ophth. Soc.* **35**:343, 1937; *Am. J. Ophth.* **21**:256 (March) 1938.

It was pointed out in this paper that the operation of scleral puncture, at the time of the occurrence of the hemorrhage, was most logical and was based on the pathologic condition that was developing. Samuels<sup>3</sup> described this process as a rupture of one of the two long posterior ciliary arteries and expressed the opinion that the seat of the rupture is at the site of entrance of the artery into the perichoroidal space. As the streaming blood drives the choroid forward, other blood vessels at the anterior and posterior aspects of the perichoroidal space may be torn by traction. If the process continues, most of the intraocular content is extruded, even through a very small wound, and the eye is lost. However, the amount of blood may be small and cause only a flat, circumscribed detachment of the uvea far forward. Unless



Sclerotomy for subchoroidal hemorrhage (after Samuels<sup>3</sup>).

there is complete extrusion of the intraocular contents, the blood does not undermine beyond the limits of the perichoroidal space. Samuels stated:

As this comes to an end posteriorly at a considerable distance from the nerve head, it is exceptional to find blood under the choroid in the posterior segment of the eye. The vortex veins, superiorly and inferiorly fix the choroid to the sclera, in the region of the equator. For this reason, the blood accumulates on the nasal or temporal side, where there is nothing to prevent the choroid from detaching itself from the sclera.<sup>3</sup>

If the hemorrhage ceases and remains confined to the perichoroidal space, a pseudomelanoma results. According to Samuels, localized

3. Samuels, B.: Postoperative Nonexpulsive Subchoroidal Hemorrhage, *Arch. Ophth.* 6:840 (Dec.) 1931.

blood remains fluid and unencapsulated for some time. It thus offers an opportunity for drainage by sclerotomy, even in late stages (figure).

Expulsive hemorrhage is ushered in by a sharp, agonizing pain in the eye, accompanied with what Ziegler<sup>4</sup> described as "convulsive or ague-like trembling" of the whole body, associated with a rapid pulse and cold, clammy perspiration. Nausea and vomiting sometimes precede the hemorrhage and at other times follow it.

This hemorrhage usually occurs in the aged person with advanced arteriosclerosis. Hypertensive vascular disease may or may not be present. It has occurred in persons who have not shown any signs of glaucoma. On the other hand, it has not occurred in some elderly arteriosclerotic patients who have had hypermature cataract removed in the presence of acute glaucoma. All observers agree, however, that the rupture of the fragile, arteriosclerotic posterior ciliary vessels is due to the sudden decrease of intraocular pressure following an intraocular operation. Some patients may show little or no generalized arteriosclerosis, with or without vascular hypertension, and yet have arteriosclerotic changes in the long posterior ciliary arteries.

The following case of expulsive hemorrhage, presumably the fourth on record, is described to point out again the value of sclerotomy in this condition, but particularly because the rupture occurred in the course of cataract extraction in a patient under thiopental sodium U. S. P. (pentothal sodium®) anesthesia.

#### REPORT OF A CASE

A woman aged 69 had a chronic noncongestive glaucoma of the wide angle type, first discovered in 1940. After a trial with miotics, an iridencleisis was performed on the right eye in 1943, with partial success. The ocular tension in each eye was controlled thereafter with miotics. Incipient cataracts were present in both eyes in 1940, and these continued to progress.

At the time she was referred to me for operation, the ocular tension was 25 mm. of mercury (Schiotz) in the right eye and 18 mm. in the left eye. Vision was reduced to good light projection in the right eye and to 20/50, with correction, in the left eye. The blood pressure was 170 systolic and 80 diastolic, and only moderate arteriosclerosis, compatible with her age, was noted on physical examination, which otherwise showed nothing significant.

On March 7, 1949 it was planned to perform a cataract extraction on the right eye and, simultaneously, an iridencleisis on the left eye. On retrobulbar injection of procaine in the right orbit, a small retrobulbar hemorrhage occurred, producing considerable proptosis of the right eye, so that the operation for cataract was abandoned. An iridencleisis on the left eye was performed without complication, and the eye healed without event. Three days later the proptosis of the right eye

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4. Ziegler: The Problem of Choroidal Hemorrhage in Cataract Extraction: Contributions to Ophthalmic Science, Jackson Birthday Volume, Menasha, Wis., George Banta Publishing Company, 1926, p. 7.

had completely receded; ocular movements were normal in all directions, and the ocular tension was 22 mm. of mercury (Schiøtz). It was considered safe to proceed with the cataract extraction.

Because of her nervousness and apprehension, it was decided to perform the operation with the patient under thiopental sodium anesthesia induced by intravenous injection. The blood pressure just prior to anesthesia was 160 systolic and 80 diastolic. It dropped to 130 systolic and 80 diastolic at the beginning of the anesthesia and did not vary, even during the hemorrhage. The pulse rate remained between 90 and 100 a minute.

As soon as the incision with the Graefe knife was made, the wound gaped, and the lens, and then the vitreous, spontaneously began to extrude. On delivery of the lens, the sutures were quickly tied. With focal illumination a small, dark brown elevation, resembling a choroidal melanoma, could be seen in the floor of the eye at 6 o'clock. It increased rapidly in size. A posterior sclerotomy in the area of the choroidal elevation was quickly made and the knife blade held twisted for three or four minutes. During this time a large amount of bright red arterial blood poured from the sclerotomy wound. As soon as the flow slackened, the vitreous protruding between the lips of the sclerocorneal wound was excised and two additional corneoscleral sutures were inserted. The pseudomelanoma was still present, although less in extent, and the eye did not appear hard to palpation. A second sclerotomy to the nasal side of the first incision was performed. Again, bright red blood flowed from the wound, but for a very short time. When it was decided that no further bleeding was taking place, the dressings were applied, and the patient was returned to her room.

During the event, she showed no signs of surgical shock, nor did her blood pressure vary. It remained between 130 and 150 systolic and 80 and 90 diastolic for a few hours after the operation and then gradually reached 175 systolic and 85 diastolic, a level which was considered the average for her. After recovery of consciousness there was no unusual pain and no nausea or vomiting. The patient was entirely comfortable twenty-four hours after operation.

At the time of the first dressing (twenty-four hours after operation) the eye pads were found to be stained with coagulated blood, and the blood clots were washed from the conjunctival sac. There was moderate edema of the lids and conjunctiva. The cornea was clear. Some blood-stained vitreous showed between the lips of the corneal wound, which gaped as far as the sutures permitted it to do. The iris was updrawn, and the pupil was filled with coagulated blood. Light perception was present, but no red reflex could be obtained. The ocular tension appeared low on palpation.

The gaping wound gradually flattened and the eye healed. The patient was discharged thirteen days later.

On examination on May 3, 1949 the corneal reflex was bright and no ocular congestion was present. The pupil was updrawn, and there was a thick membrane in the pupillary space. There was no red reflex. The tension measured 14 mm. of mercury (Schiøtz), and she had good light projection.

#### COMMENT

The experience in this and in other cases warrants the immediate use of sclerotomy in the event of expulsive hemorrhage. The fact that such a disaster can occur during anesthesia with thiopental sodium should be emphasized. The usual signs of pain and surgical shock are

missing. The surgeon should suspect its occurrence in these circumstances when the lens begins to present as soon as the incision is made, and he should be confirmed in his suspicions when vitreous begins to deliver as soon as the lens is extruded. He should carefully search with oblique illumination, and perhaps with the ophthalmoscope as well, for a "pseudomelanoma" and perform the sclerotomy in this area. It would be better, I think, to make a trephine opening in the sclera and thus allow all blood to escape as long as it will. A knife incision closes rapidly. Verhoeff suggested that small, triangular incisions be made, the apex of the triangle being excised to afford continuous exit to the blood.

It is interesting to note that during the hemorrhage there was no alteration in the patient's blood pressure. Furthermore, the blood pressure was considerably lowered during the anesthesia. This suggests that an elevated blood pressure per se plays no part in the production of this condition. The fact that the patient's left eye had been operated on (iridencleisis) but three days before, without any untoward event, supports the premise that a purely uniocular, local fragility (arteriosclerosis) of the posterior ciliary arteries was present and was responsible for the rupture of the vessels when the intraocular pressure was somewhat abruptly lowered. It is difficult to surmise what role, if any, the previous glaucoma played, for it was bilateral. It was more advanced, however, in the right eye.

It is also difficult to evaluate the part played by the retrobulbar hemorrhage subsequent to injection of procaine three days prior to the cataract operation. I am certain that the retrobulbar pressure had become normal by the time of operation. The proptosis had completely disappeared and the ocular motility had been restored to normal at the time of operation. It is possible, however, that the proptosis of the eye had stretched the sclerotic posterior ciliary arteries, with resultant deleterious effect, and had increased thereby their fragility. However, expulsive hemorrhage has occurred in cases in which retrobulbar injection of procaine has been used without retrobulbar hemorrhage and in the old days before retrobulbar anesthesia was even considered.

From experience in this and in other cases, the logical conclusion is that (a) a trephine should be on every cataract instrument tray, (b) a sterile trephine or cataract knife should be ready for use on every dressing tray in the event that there is a delayed expulsive hemorrhage and (c) every ophthalmic surgeon and resident should be prepared for instant action in the event of a threatened expulsive hemorrhage.

## INTRACAPSULAR EXTRACTION OF CATARACTA COMPLICATA ACCRETA AFTER IRIDOCYCLITIS AND GLAUCOMA

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THE OPERATION for cataracta accreta following iridocyclitis, before the introduction of the intracapsular method by Arnold Knapp, was a source of anxiety to the surgeon and of danger to the patient's eye. Every surgeon who had to operate extracapsularly in cases of this type knows by experience how many eyes were destroyed by the recurrence of iridocyclitis and the hypotony and glaucoma often connected with it. Experienced cataract surgeons, therefore, because of the unfavorable prognosis, declined to undertake extraction in such cases, either on principle, thus condemning the patient to lasting practical blindness, or because they followed the advice of Axenfeld.<sup>1</sup> This author suggested that in such cases one first do a total iridectomy, if it had not already been done, and, with Weber's loop, extract the cataracta complicata as a whole, if possible, so as to save the eye the postoperative recurrence of iridocyclitis caused by remnants of the lens. Therefore, the trauma of loop extraction of the lens used to be the lesser evil in operations on such eyes. I myself can remember, from the days when I was an assistant, many an eye in which the operation was followed by lingering iridocyclitis, occlusion of the pupil, opacity of the vitreous and, occasionally, atrophy of the globe.

If, formerly, surgeons, such as Arnold,<sup>2</sup> Gutmann,<sup>3</sup> Proksch<sup>4</sup> and Seefelder,<sup>5</sup> advocated the extracapsular extraction of cataracta complicata, they thought of this cataract in a broad sense, such as the cataracts following corneal processes, retinitis pigmentosa, detachment of the retina and macular degeneration. Among these, the cataracts following iridocyclitis form the smallest group.

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From the First University Eye Clinic.

1. Axenfeld, T.: Die Extraktion nach Iridocyclitis, Deutsche. Ophth. Gesellsch., Heidelberg, 1924.

2. Arnold: Arch. f. Augenh. 25:41, 1892.

3. Gutmann: Die operative Behandlung der Katarakta complicata, Arch. f. Augenh. 40: 1900.

4. Proksch, M.: Ueber operative Aussichten bei komplizierter Katarakt, Ztschr. f. Augenh. 92:129, 1937.

5. Seefelder, R.: Zur Operation des komplizierten Stares, Ztschr. f. Augenh. 57:12, 1925.



It, therefore, was to the credit of Arnold Knapp to have been the first (in 1910) to recognize the value of intracapsular extraction and to have carried it out systematically. In 1915 Knapp<sup>6</sup> reported on his first 100 intracapsular extractions. His method differed in one essential point from the intracapsular extraction of Stanculeanu, which was published in 1911 and in which the lens was grasped in the middle of the pupil with the forceps and luxated. Knapp, from the very beginning, recommended the grasping of the lens capsule near the lower rim and the tumbling of the lens. This method, modified by Elschinig, was adopted by nearly all ophthalmologists in the following two decades. That A. Knapp originally discarded the Kalt forceps after luxation of the lens and extracted the loosened lens by pressure exerted on the lower portion of the limbus lessens in no way the credit due him. Today, cataract surgeons follow the method proposed by Elschinig and grasp the deep portion of the lens and luxate and tumble it without removing the forceps.

Soon this intracapsular extraction was tried with different kinds of cataracta complicata, and its advantages were recognized. From the historical point of view, one can understand Elschinig<sup>7</sup> when he spoke of the "triumph of the intracapsular method," inasmuch as good results were produced in nearly 100 per cent of cases when this technic was applied to cataracts following cyclitis. Success with the intracapsular extraction of cataract after iridocyclitis was subsequently reported by Arruga,<sup>8</sup> Bonnet and Paufigue,<sup>9</sup> Davis,<sup>10</sup> Gaily,<sup>11</sup> Jaeger,<sup>12</sup> Knapp,<sup>13</sup> Krucckmann,<sup>14</sup> Lindner,<sup>15</sup> Passow,<sup>16</sup> Paufigue,<sup>17</sup> Sjövall,<sup>18</sup> Sinclair,<sup>19</sup>

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6. Knapp, A.: Report of One Hundred Successive Extractions of Cataract in the Capsule after Subluxation with the Capsule Forceps, *Arch. Ophth.* **44**:1, 1915.

7. Elschinig, A.: *Die intrakapsulare Starextraktion*, Berlin, Julius Springer, 1932.

8. Arruga, H.: Les avantages et les inconvenients de l'extraction totale de cataracte, *Bull. et mém. Soc. franç. opht.* **48**:218, 1935.

9. Bonnet, P., and Paufigue, L.: Cataracte: La valeur de l'extraction totale, *Bull. et mém. Soc. franç. opht.* **51**:439, 1938.

10. Davis, F. A.: Personal Experiences with Intracapsular Cataract Extractions, *Arch. Ophth.* **19**:867 (June) 1938.

11. Gaily, W.: Some Problems Encountered in Cataract Surgery, *Am. J. Ophth.* **21**:855, 1938.

12. Jaeger, E.: Erfahrungen mit der intrakapsularen Starextraktion, *Klin. Monatsbl. f. Augenh.* **1**:316, 1940.

13. Knapp, A.: Present State of the Intracapsular Cataract Operation, *Arch. Ophth.* **38**:1 (July) 1947.

14. Krucckmann, E.: La extracción intracapsular de la catarata, *Rev. cubana de oto-neuro-oftal. oftal.* **1**:24, 1932.

Wright,<sup>20</sup> Urbanek<sup>21</sup> and others. But the reports did not go beyond general statements, such as, "with cataracta complicata after the iridocyclitis the intracapsular extraction was successful nearly without exception."<sup>15</sup> Horvath,<sup>22</sup> Arruga<sup>23</sup> and Mānes<sup>24</sup> referred to the operation for "choroidal cataract," by which they undoubtedly meant cataracta complicata after iridocyclitis.

Contrary to the view of these authors, other surgeons, such as Appleman<sup>25</sup> and Cosmetatos,<sup>26</sup> still advise against intracapsular extraction of cataract with iridocyclitis and either prefer the extracapsular method or refrain from any operation. Moron y Ruiz<sup>27</sup> proposed total iridectomy in cases of cataracta complicata after iridocyclitis, followed by slitting the upper equator of the lens with Graefe's knife and then extraction, one branch of the straight indented forceps being laid into the lens underneath the capsule and the other on the surface of the anterior capsule of the lens, so that the lens is extracted with the capsule. He reported a 10 per cent loss of vitreous in this procedure.

Since the opinions of Elschnig<sup>7</sup> met with opposition in the literature, and since extensive serial examinations are still lacking, I shall report on an unselected series of 105 intracapsular extractions for cataracta

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15. Lindner, K.: Ueberblick über die im Jahre 1938 mit meiner geänderten Operationstechnik ausgeführten Staroperationen, *Klin. Monatsbl. f. Augenh.* **103**: 156, 1939.

16. Passow: Bericht über die intrakapsuläre Starextraktion, *Klin. Monatsbl. f. Augenh.* **100**:764, 1938.

17. Paufigue, L.: L'iridectomie préparatoire dans l'extraction capsulo-lenticulaire de la cataracte, *Bull. Soc. d'opht. de Paris* 1936, p. 115.

18. Sjövall, H.: Starextraktion in der Kapsel, *Svenska läk.-tidning* **29**:677, 1932.

19. Sinclair, A. H. H.: Presidential Address, *Tr. Ophth. Soc. United Kingdom* **52**:37, 1933.

20. Wright, R. E.: Lectures on Cataract: IV. Posterior Segment Complications in the Postoperative Period; Some Difficult Extractions, *Am. J. Ophth.* **20**:376, 1937.

21. Urbanek, J.: Massnahmen zur Verhütung von Komplikationen während und nach der intrakapsulären Starausziehung, *Klin. Monatsbl. f. Augenh.* **106**:129, 1941.

22. Horvath, B.: Operation einer Flächenhaft angewachsenen Katarakt, *Klin. Monatsbl. f. Augenh.* **103**:120, 1939.

23. Arruga, H.: Die Extraktion der komplizierten Katarakt, *Verhandl. d. Fourteenth internat. Kongr. Ophth. (Madrid)* **1**:73 and **4**:429, 1934.

24. Manes, A. J.: Die Operation der Chorioidalkatarakt, *Arch. de oftal. de Buenos Aires* **10**:671, 1935.

25. Appleman, L. F.: Intracapsular Cataract Extraction: Report of a Further Series of Cases, *Arch. Ophth.* **19**:548 (April) 1938.

26. Cosmetatos, G. F.: Einige Bemerkungen zur intrakapsulären Kataraktextraktion, *Ophthalmologica* **101**:1, 1941.

27. Moron y Ruiz: La operación de la catarata complicada: su extracción con pinzas, *Med. españ.* **9**:323, 1943.

complicata accreta after iridocyclitis which were performed in my clinic from 1945 to 1949. My colleagues and I now attempt intracapsular extraction for nearly all kinds of cataracts except those in persons under 30 years of age. Eighty operations of this series were carried out by me personally and 25 by my assistants.

#### OPERATIVE METHOD

A 5 or 10 per cent solution of cocaine with epinephrine is instilled and akinesis induced with subconjunctival and retrobulbar injection; a traction suture (*Zugelnäht*) is placed through the superior rectus muscle; a "preplaced" suture (*Liegard*) is used, and then a flap section of over two fifths of the conjunctiva is made with a Graefe knife. Posterior synechias are broken by introduction of a spatula behind the iris as far as the root of the iris with preservation of a round pupil if possible; but if there is an occluding membrane, an extensive total or peripheral iridectomy is first done, so that after detaching the synechias and the pupillary membrane one can grasp the lens in its lower half with the Arruga forceps. If a posterior synechia exists, I first try to make a small peripheral iridectomy at 12 o'clock and then bring the spatula through this opening behind the iris, in order to break the synechia on the posterior surface. In such cases, after the posterior synechia is detached, one should try to perform a total iridectomy or an iridotomy so as to be able to grasp the lens below. If a severe hemorrhage should occur from the vessels of the iris or of the occluding membrane, the operation is interrupted and the intracapsular extraction postponed to a later date. Otherwise, the lens is grasped with the Arruga forceps in its lower half and tumbled or extracted upright under pressure with the spatula at 6 o'clock. Only if the cataract proves to be luxated or subluxated do I grasp the capsule above in the region of the iridectomy, after lifting the iris near the equator above.

The luxation of the lens is usually successfully accomplished by the detaching maneuver with the spatula or as a result of atrophy of the zonule of Zinn due to the cyclitic process. Only when the lens adheres to the anterior limiting membrane of the vitreous body, a condition that is rarely encountered, may the extraction become difficult and vitreous escape. Sometimes a thread of vitreous hangs on the posterior surface of the lens, and this vitreous must be cut off immediately with the deWecker scissors. One, therefore, should always perform the extraction of complicated cataract slowly, while observing every detail minutely.

If extraction takes place with a round pupil, the usual peripheral iridectomy is done. The section removed should not be too small. Then follow the dressing of the wound, the tying of the preplaced suture and the placing of two hair sutures on the temporal and nasal parts of the conjunctival flap.

If the cataract is extracted behind an inflammatory pupillary membrane (*occlusio pupillae*), a careful vertical section of the occluding membrane may be made with the deWecker scissors or the section of this membrane left until later. Operation is followed by twenty-four hours of rest in bed and bandaging of both eyes; the eye operated on is bandaged for eight days, with daily control, and the patient is dismissed on the twelfth to the fourteenth postoperative day.

As a rule, after such intracapsular extraction, the patient experiences an astonishing absence of irritation of the eye. On the other hand, some eyes with iridocyclitis show after operation a hyphema which is slow to resorb, a Tyndall sign, pronounced traumatic opacity of the cornea or swelling and increase in density of old corneal scars.

In any case, by a successful intracapsular extraction, one saves the eye from the recurrent iridocyclitis which nearly always develops after extracapsular extraction, from dangerous hypotony and from the subsequent discussion of secondary cataract, never without risk to cyclitic eyes.

#### OBSERVATIONS

The 105 operations for cataracta complicata, to be reported here, were distributed as follows:

Condition	No. of Eyes
Cataracta complicata after iridocyclitis.....	63
Cataracta complicata after operation for glaucoma with posterior synechias .....	30
Cataracta traumatica after iridocyclitis traumatica.....	5
Cataracta complicata with Fuchs's heterochromia.....	5
Cataracta complicata and aplasia of the iris.....	2

The formation of synechias was common in the first three groups, in which more or less dense adhesions of the iris to the lens were present. In group 1 the synechias formed after endogenous, usually tuberculous, iridocyclitis; in group 2 the iritis occurred after Elliot's trephination, iridencleisis or iridectomy, and in group 3 the iritis followed a perforating injury. In group 4 cataract followed a lingering uveal disorder (heterochromia), and in group 5, it was superimposed on a congenital inferiority of the uveal tissue (aplasia of the iris). In the last two groups no posterior synechia was noted.

All the patients were examined eight weeks after the cataract extraction, and the majority of the patients also at a later date. The period of observation in the early cases was fifty-four months, and that in recent cases, two months. In a few cases no postoperative examination could be undertaken after the cataract operation. The vision recorded is that which was found at the latest postoperative examination, even when the visual acuity had been better at an earlier examination.

In 16 cases the cataract operation was undertaken on both eyes, and in 73 cases, on only one eye. Among the 89 patients there were 8 one-eyed persons.

Of the 89 patients, 36 were men and 53 women. The age distribution was as follows:

Age, Yr.	No. of Patients
10-19 .....	1
20-29 .....	1
30-39 .....	3
40-49 .....	10
50-59 .....	17
60-69 .....	26
70-79 .....	29
Over 80 .....	2
Total .....	89

GROUP 1.—*Cataracta Accreta After Iridocyclitis (63 eyes).*—Of these 63 eyes, there were 2 with cataracta complicata after sympathetic ophthalmia, 1 with endogenous hypopyon iritis of unknown cause and 60 with tuberculous iridocyclitis, of which one group showed corneal opacities after phlyctenular keratitis or accompanying tuberculous choroiditis.

The duration of iritis may be summarized as follows:

Duration of Iritis, Yr.	No. of Eyes
1- 9 .....	14
10-19 .....	15
20-29 .....	13
30-42 .....	18
Unknown .....	2

Of the patients with iritis, 17 were men and 33 women, a total of 50 patients, representing 63 eyes with cataract.

Aspect of the Cataracts: In 61 eyes the cataracts in the posterior cortex were more densely opaque than those in the anterior cortex. Therefore, except for incipient cataracts, they were of the “rosette” type. In 1 eye (with hypopyon iritis) a spotted thickening of the anterior capsule was found; in a second a ring-shaped ridge of the anterior capsule with capsular folds was noted.

Results of Operation: The results of intracapsular cataract extraction for the 63 eyes are tabulated as follows:

No. of Eyes	Result	
51 .....	+	} 57 eyes, 90.4% (intracapsular)
3 .....	±	
3 .....	∓	
6 .....	—	} 6 eyes, 9.6% (extracapsular)

The sign  $+$  indicates that the cataract had been extracted in the capsule without any complication;  $\pm$ , that the capsule, though it ruptured in a circumscribed spot during the extraction, was nevertheless extracted with the cataract;  $\mp$ , that the capsule subsequently could be grasped and removed as a whole, and  $-$ , that the lens eventually had to be removed without the capsule. In all cases the final result was complete removal of the lens. This result was confirmed in all cases by examination with the slit lamp.

In 6 cases complications arose during or after the cataract operation. In case 4 a vitreous strand which hung on the posterior surface of the lens had to be cut off with the scissors when the lens was extracted. No loss of vitreous occurred. Vision was 6/8 and ability to read Jaeger's test type 1. In an eye with old sympathetic ophthalmia (case 32) there were loss of vitreous after the section, luxation of the cataract toward the vitreous and, on the fifth day, endophthalmitis, with consequent enucleation. In case 58 serous iritis, probably of allergic nature, developed eight days after the extraction of the cataract (after both operations, serious eczema, resulting from plaster, occurred over the whole face, the neck and the chest), and vision was 6/12 and ability to read Jaeger's test type 1. In case 75, in which at the time of the extraction the lens still showed fresh precipitates, four days after extraction of the lens a slight fibrinous exudation occurred in the anterior chamber. This exudate promptly disappeared after two injections of milk. Final vision was 6/60 and ability to read Jaeger's test type 10, loss of acuity being due to tuberculous retinitis proliferans in the macular region.

In the remaining 57 cases, in spite of the fact that in all cases posterior synechias had to be detached with the spatula, sometimes with hemorrhage into the anterior chamber, the cataract extraction progressed without untoward incidents, and postoperative healing was excellent. It is noteworthy that in 1 case (case 32, old sympathetic ophthalmia) there was loss of vitreous, followed by endophthalmitis, which led to the loss of an eye. In no case was there postoperative prolapse of the iris, because in most cases a broad peripheral or total iridectomy was performed for detachment of the posterior synechia.

Postoperative vision in these 63 eyes was as follows:

Visual Acuity	No. of Eyes
6/6-9/9 .....	17
6/12-6/18 .....	9
6/24-6/36 .....	14
6/60-3/60 .....	7
Less than 3/60 .....	7
Blind .....	2
No postoperative examination .....	7
Total .....	63

The resulting vision appears unfavorable as compared with that after intracapsular operation for senile cataract. This poor result was not the fault of the method of operation but must be attributed to the chronic iridocyclitis with its opacities in the vitreous (often existing for ten to forty years), the complicating tuberculous changes in the eyeground or scars on the cornea, often dating back to childhood, the sequelae of phlyctenular keratitis. Nevertheless, 40 of the 63 eyes had useful vision of 6/6 to 6/36, and only 14 eyes had visual acuity of 6/60 or less. Two eyes were blind.

Of the 14 eyes with vision of less than 6/60, 13 had the cataract extracted in the capsule without complication and 1 had the cataract extracted with the capsule, though the latter was ruptured. This indicates that the poor vision was due not to the operation but to iridocyclitis.

In the 7 cases with vision of 6/60 to 3/60, the causes of the poor function were as follows: opacity of the vitreous with constantly recurring iritis and secondary optic nerve atrophy (case 13); serious chorioretinitis diffusa centralis of long standing (case 16); very dense opacity of the vitreous, obscuring the fundus (case 19); opacity of the vitreous and secondary optic nerve atrophy (case 35); dense opacity of the vitreous, diabetic changes in the eyeground and glaucoma (case 54); contraction of the visual field close to the fixation point following secondary glaucoma (case 60), and central choroiditis combined with corneal opacification (case 103).

Of the 7 eyes with less than 3/60 vision, 6 were of intracapsular extraction without complication, and 1, of rupture of the capsule, with eventual intracapsular delivery, all without complications. The causes of the poor vision were dense opacity of the vitreous and secondary optic nerve atrophy (case 6); corneal opacity, dense opacity of the vitreous and central choroiditis (case 15); disseminated choroiditis and glaucomatous optic atrophy (cases 20 and 21); dense vitreous opacity obscuring the fundus (case 37); diabetic retinitis and vascular hypertension (case 55), and extremely dense opacities of the vitreous caused by consistently recurring iridocyclitis (case 98).

Of the 2 blind eyes, 1 was the eye with sympathetic ophthalmia aforementioned (case 32). In this case, when the cataract was extracted loss of vitreous occurred and a loop extraction was necessary. Subsequently endophthalmitis developed, and the eye was enucleated on the fifth day. The second eye was that of a woman aged 36 with severe tuberculous iridochoroiditis, whose left eye had postoperative vision of 3/36 and ability to read Jaeger's test type 12. Twenty-three months later, because of an unexplained serious hemorrhage in the anterior chamber during pregnancy, the eye became blind, with the signs of xanthomatosis bulbi. The eye had been quiet for twenty-three months following the operation.

Of the 7 eyes not examined after operation, 2 had vision of 6/12 and 6/24, respectively, fourteen days after operation; the other 5 eyes had vision of less than 6/60 because of dense vitreous opacities (2 cases), central choroiditis (1 case), glaucomatous optic nerve atrophy (1 case) and secondary optic nerve atrophy and vitreous opacity (1 case). In 6 of these eyes intracapsular extraction was done without complications (+); in 1 eye the lens was eventually extracted extracapsularly (—).

Summary: Of 63 eyes with moderately severe iritis of from one to forty-two years' duration, the cataracta complicata could be removed by intracapsular extraction in 90.4 per cent (57 cases). In 9.6 per cent the capsule ruptured and the benefit of operation (cataract with sympathetic ophthalmia) was destroyed by endophthalmitis; another eye twenty-three months later was found to have gone blind with the signs of hemorrhagic iridocyclitis, not associated with the cataract operation. In 5 eyes there were slight postoperative complications (hyphema, iridocyclitis). In no case did the iris prolapse. The defect in the final vision attained by the cataract operation is explained in all cases by the preoperative iridocyclitis and its associated complications.

I should like to emphasize that no eye was destroyed by postoperative iridocyclitis or hypotony.

GROUP 2.—*Cataracta Accreta After Operations for Glaucoma (30 eyes).*—The posterior synechias which were present in these 30 eyes (27 patients) should be thought of as complications following operations for glaucoma, such as Elliot's trephining, Graefe's iridectomy and iridencleisis. In half the cases there was formation of moderate, and in the other half of extensive and persistent, synechias, all of which had to be detached before the intracapsular extraction.

Of the 27 patients, with 30 cataract extractions, 13 were men and 14 women. The age distribution was as follows:

Age, Yr.	No. of Patients
40-49 .....	1
50-59 .....	2
60-69 .....	9
70-79 .....	14
Over 80 .....	1
Total .....	27

The distribution of cataract with respect to the type of glaucoma was as follows:

Type of Glaucoma	No. of Eyes
Acute inflammatory .....	18
Chronic noninflammatory .....	11
Capsulolenticular .....	1
Total .....	30



It must therefore be pointed out that most cataract operations had to be performed on eyes which had previously passed through acute inflammatory glaucoma. In such eyes the tendency to formation of synechia is greater than in eyes with chronic noninflammatory glaucoma.

At the time of the cataract extraction, the glaucoma had dated back as follows:

Duration of Glaucoma, Yr.	No. of Eyes	Duration of Glaucoma	No. of Eyes
½	1	11	2
1	6	12	1
2	6	14	1
3	5	15	2
5	2	17	1
6	1	23	1
8	1		

The cataracts must, for the greater part, be considered as senile. since both the posterior and the anterior cortex were involved. On the other hand, the nuclear cataract, particularly the brunescens type. may be considered as due to glaucoma itself. Furthermore, among these 30 cataractous lenses, 2 were subluxated after trauma, 2 were subluxated after iridectomy and 1 was a milky cataract.

The relation of posterior synechias to operation for glaucoma was as follows:

	No. of Eyes
After one operation for glaucoma .....	22
After iridencleisis .....	3
After iridectomy .....	14
After Elliot trephining .....	3
After cyclodialysis .....	2
After two operations for glaucoma .....	5
After iridectomy and cyclodialysis .....	4
After Elliot trephining and cyclodialysis .....	1
After operations for glaucoma .....	3
After Elliot trephining, iridectomy and cyclodialysis .....	1
After Elliot trephining, cyclodialysis and trephining cyclo-	
dialysis .....	1
After Elliot trephining, cyclodialysis and posterior tre-	
phining of the sclera .....	1

Results of Operation: In 30 intracapsular cataract operations, which had in every instance been preceded by an ample separation of the posterior synechias by means of the spatula, the results were as follows:

Operation	No. of Eyes	
Intracapsular; no complication (+).....	21	} 25 eyes, 83.33%
Intracapsular; localized rupture but operation com- pleted (±) .....	2	
Intracapsular; rupture but capsule grasped and reserved as whole (≡).....	2	
Operation concluded by extracapsular method (—)	5	} 16.66%

Thus, the intracapsular operation was successful in 83.33 per cent of the cases; in 16.66 per cent the operation had to be concluded extracapsularly. As in all operations for glaucoma, with the exception of the 2 cases with primary cyclodialysis, a coloboma of the iris was already present, and the spatula could be directed for the detachment of the posterior synechia through the coloboma behind the iris. In a case of ring-shaped synechias after cyclodialysis a total, and in the second case, with slight posterior synechias, a peripheral, iridectomy was done before the detachment of the posterior synechias.

In 2 cases an existing occluding membrane of the pupil was dissected after intracapsular extraction of the lens by means of the deWecker scissors.

Postoperative complications occurred in 3 eyes: In 1 eye (case 22; intracapsular extraction, no complication [ + ]) slight loss of vitreous and a slight iridodialysis occurred because of dense adhesions of the lens below with the posterior surface of the iris or the ciliary body. Final vision was 6/18 and ability to read Jaeger's test type 2. In 1 eye (case 50) (operation concluded by extracapsular extraction [ — ]) there was considerable hemorrhage into the anterior chamber. Final vision was 2/60, and inability to read Jaeger's type because of glaucomatous contraction of the visual field beyond the fixation point. In 1 eye (that of a man aged 79, with glaucoma existing for twenty-five years; uncomplicated intracapsular [ + ] operation) a hyphema developed, followed by chemosis and ingrowth of deep vessels into the cornea from above. Vision six months after the cataract extraction was limited to light perception at 6 meters and good projection. There was a membrane in the coloboma.

A woman of 78 (uncomplicated intracapsular extraction in both eyes) died of cardiac insufficiency five days after the operation on the second eye.

The tension of eyes with glaucoma after the intracapsular cataract extraction remained on the same level as before the operation, that is, within normal limits. In 1 case (case 99) the eye operated on (intracapsular extraction [ + ]) became soft (10 mm. of mercury), but the vision after three years' observation remained 6/36 with ability to read Jaeger's type 5. In a case in which vision after intracapsular extraction ( + ) had been 6/18 and ability to read Jaeger's type 2 (case 100), the eye was found to have become blind because of increase of tension when a control examination was made three years later, and this eye was destroyed by a seriginous ulcer.

In all cases during the cataract section the trephining or iridencleisis scar was taken into account and the filtration scar avoided, the knife being brought forward in front of the scar through the sclera and the cataract incision concluded upward conjunctivally. In this manner it

is possible to avoid changing the appearance and function of a trephining or iridencleisis scar by the cataract incision. For a scar after Graefe's iridectomy I place the cataract incision, if possible, peripheral to the iridectomy scar, so as to reopen the angle of the anterior chamber.

Postoperative vision in 30 eyes was as follows:

Visual Acuity	No. of Eyes	
6/6-6/9 .....	7	} 22 eyes, 73.33%
6/12-6/18 .....	9	
6/24-6/36 .....	6	
6/60-3/60 .....	0	
Less than 3/60 .....	2	
Hand movements .....	2	
Blind .....	1	
No examination .....	3	
Total .....	30	

In 73 per cent of the glaucomatous eyes on which intracapsular extraction was performed, the vision obtained was in accord with what could be expected from the glaucomatous field of vision and the changes in the eyeground. In none of these eyes was poor vision the result of the intracapsular extraction; it was due only to the glaucoma.

Of the 2 glaucomatous eyes with less than 3/60 vision after cataract extraction, the glaucoma had existed for twenty-five years in 1 eye (case 50); the lens had been extracted by the extracapsular method (—), and a deep glaucomatous excavation and only a temporal field were present. In the second eye (case 43) glaucoma was of two years' duration, with a history of acute exacerbation (+ extraction) and total glaucomatous excavation.

In the 2 cases with vision limited to perception of hand movements and to light perception at 6 mm., respectively (cases 31 and 63, both with uncomplicated [ + ] intracapsular extractions of the lens), the poor final vision was due to glaucoma, with optic nerve atrophy, which had lasted for decades.

In the case of blindness (case 100) sight was lost because of continued increase of tension three years after the intracapsular ( + ) extraction. For 3 eyes (cases 67, 85 and 104) no postoperative examination was made.

In the entire series of 30 intracapsular extraction of cataracta accreta in glaucomatous eyes there was not a case in which vision was favorably influenced by the cataract operation itself.

Summary: Of 30 eyes with glaucoma of long duration and cataracta accreta, the cataract was extracted in the capsule in 83.33 per cent; in 16.66 per cent the operation had to be concluded by the extracapsular method. In all cases the posterior synechias were detached by means of the spatula, which had to be carried out as far back as the root of

the iris. In all cases the final vision was essentially improved by the cataract operation. Poor vision was due to optic nerve atrophy associated with glaucoma. There were no serious complications as a result of the cataract operation in any case. With the exception of 2 cases, tension remained unchanged after the cataract operation; in 1 case there was hypotony of 10 mm. of mercury; in a second case the eye, three years after the intracapsular cataract extraction, was found on postoperative examination to have become blind from glaucoma.

GROUP 3.—*Cataracta Accreta After Iritis Traumatica (5 eyes).*—Again, in cases of cataracta traumatica, before intracapsular extraction can be performed, the posterior synechias must be detached carefully with the spatula. The cataract extraction should take place no less than six months after the perforating injury, i. e., after disappearance of the intraocular inflammation due to the trauma. The 5 cases are summarized as follows:

CASE 10.—Injury of the left eye by the handle of a spade in 1912. Iridocyclitis with posterior synechia and cataracta complicata. Uncomplicated intracapsular cataract extraction (+) in 1945. Final vision with correction 6/6 and ability to read Jaeger 1.

CASE 87.—Extraction of an intraocular foreign body by magnet in 1922. Cataracta traumatica and iridocyclitis. Intracapsular extraction, uncomplicated (+) in 1949; escape of fluid vitreous at the time of incision; luxation of the lens toward the vitreous body after detachment of the synechias. Total iridectomy; extraction by grasping of the lens above. Vision 6/24 and ability to read Jaeger 3. Persistence of the hyaloid artery.

CASE 97.—Injury of the left eye from a piece of wood in 1939; iridocyclitis. Cataracta accreta in 1942. In 1946 intracapsular cataract extraction with peripheral iridectomy (+); excision of thread of the vitreous body hanging from the lens. Final vision with correction 6/8 and ability to read Jaeger 1.

CASE 101.—Injury of the right eye by a splinter of a grenade, in Africa (1943). Adherent leukoma, iridocyclitis and traumatic cataract with crystal formation. Intracapsular cataract extraction (±) with peripheral iridectomy in 1946. On detachment of the posterior synechia the capsule of the lens was torn in the region of the leukoma. Expression of the cataract and subsequent extraction of the capsule. Vision with correction 6/8 and ability to read Jaeger 1.

CASE 105.—Perforating injury of the left eye by glass with iritis and traumatic cataract in 1927. Anterior and posterior synechias. In 1948 intracapsular extraction with peripheral iridectomy (—): Dissection of the anterior synechia in the anterior chamber; then, during detachment of the posterior synechia, rupture of the capsule, with partial extraction. Final vision with correction 6/18 and ability to read Jaeger 1. Corneal scar.

Of the 5 cases of complicated cataract after performing injury, intracapsular extraction could be done in 4 (uncomplicated [ + ] in 3 cases and rupture of the capsule with eventual removal [ ± ] in 1). Vision after the extraction of the cataract was 6/6 in 1 case; 6/8 and

ability to read Jaeger's type 1 in 1 case, because of central cornea scar; 6/8 and ability to read Jaeger's type 1 in 2 cases, and 6/24 and ability to read Jaeger's type 3 in the last case, because of opacities and liquefaction of the vitreous.

The intracapsular extraction, therefore, rendered excellent service in these 5 cases of traumatic cataract.

GROUP 4.—*Intracapsular Extraction of Cataract with Heterochromia (5 eyes).*—There were 3 men (aged 41, 48 and 18, respectively) and 2 women (aged 58 and 57, respectively) with Fuchs's heterochromia of the iris, precipitates scattered over the entire posterior surface of the cornea and cataract in the lighter eye. In 1 case corneal maculas followed eczematous keratitis. There were no posterior synechias, but diffuse atrophy of the iris was present in 2 cases.

In 4 cases the cataract could easily be extracted intracapsularly (+); in the case of the youngest patient (aged 18) the capsule was so slippery that capsule forceps could not grasp it. The capsule had, therefore, to be torn open with the toothed forceps and the cataract removed extracapsularly. There were no complications in any of the cases.

Vision with correction was 6/6 and ability to read Jaeger's type 1 in 4 cases; in 1 case, because of vitreous opacity, it was 6/18 and ability to read Jaeger's type 2.

It is advisable, therefore, in cases of cataract with heterochromia to use the intracapsular method. It is usually successful in cases of this type. I encountered slippery capsules only in some cases of perinuclear cataract, as in the case mentioned. In these cases an attempt at intracapsular extraction should be made, the lens being grasped by the equator above.

GROUP 5.—*Intracapsular Extraction in Aplasia of the Iris (2 eyes).*—These 2 cases were included in this paper because these rare cataracts owe their origin to a congenital fault of the uveal tissue. Such cataracts can occur at a comparatively early age.

CASE 1.—A woman aged 33 had had reduced vision since her childhood. Operation for cataract was performed on the right eye at the age of 30 and on the left eye in 1945. Escape of liquid vitreous followed the cataract incision. Total iridectomy and intracapsular extraction, uncomplicated (+), were performed. Fourteen days after the extraction vision was 6/24 and ability to read Jaeger's type 4. No postoperative examination was made.

CASE 22.—A woman aged 55 had had poor vision since the age of 7 years. Cataract extraction on the left eye in 1934 was followed by choroiditis. Vision was 6/36 and ability to read Jaeger's type 5. In 1946 intracapsular cataract extraction, uncomplicated (+), was performed on the right eye, with subsequent high myopia. Vision with correction was 6/8 and ability to read Jaeger's type 1.

In cases of cataracta complicata of this type the intracapsular method of extraction is indicated because, apparently as a result of the uveal disturbance, the zonule of Zinn degenerates prematurely and the intra-

capsular extraction can be successfully performed at a comparatively early age. In some of these cases, however, one must reckon with complications in the vitreous.

Of the 98 eyes with cataracta complicata in the first three groups, 86, or 87.7 per cent, could be operated on intracapsularly. When Elschmig, in his monograph, spoke of cataracts in cyclitic eyes and mentioned a 100 per cent chance of success, his statement was based only on an impression, not on figures. We must therefore curb our enthusiasm, but we may be confident that in the technic of intracapsular cataract extraction, first practiced by Arnold Knapp, we possess not only a method for the operation of senile cataract, but a procedure that in nearly 88 per cent of cases can be carried out successfully in dealing with cataracts following iridocyclitis. Formerly, it was much more difficult to operate on cataracts of this type, no matter whether the iritis was endogenous or exogenous (due to perforating injury or by operation for glaucoma). Extracapsular cataract operation on such eyes often was followed by a serious recurrence of the iritis or by a return of the glaucoma.

#### COMMENT

The present series of nearly 100 intracapsular cataract operations for cataracta accreta demonstrates that eyes with such previous severe damage tolerate the intracapsular extraction exceedingly well, that the healing of the wound proceeds smoothly, that the number of complications is not greater than in operations for senile cataract and that in this series of 105 operations the eye was destroyed by an infection in only 1 case. This was the case of sympathetic ophthalmia after perforating injury of the other eye which the patient underwent at an early age. The vitality of the eye was seriously damaged and the infection could not be overcome.

According to A. Knapp and Elschmig, the intracapsular method also makes possible early operation on such cataracts. In eyes with vision already impaired by iritis or glaucoma, operation is especially important, for even the slightest opacity of the lens can blur the remaining vision of such eyes more than would be the case with uncomplicated cataracts. One should, therefore, operate for cataracta complicata with iridocyclitis and glaucoma as soon as possible, intracapsularly. But with all justified optimism, one should always bear in mind those uncertainties which necessarily accompany intracapsular extraction of cataracta accreta.

In spite of careful examination of eyes with iridocyclitis by means of the slit lamp, one cannot see every adhesion between the lens and the iris. Even after most careful separation of the posterior synechias with the spatula, the lens can "hang" when extraction takes place, and it is sometimes very difficult to tumble it or extract it in an upright

position. Pigment deposits which are often found on the periphery of the lens after successful extraction prove the presence of previously unseen synechias which the spatula could not reach. On the other hand, the lens is sometimes actually walled into a cyclitic membrane and can be extracted with surprising ease. Furthermore, one is often surprised at the easy extraction of the lens in an eye with long-standing glaucoma as soon as the posterior synechias have been detached.

Loss of vitreous must always be expected in eyes with uveal disease. Fluid vitreous may escape until the sclera collapses. The resulting sliding back of the lens can on occasion render intracapsular extraction more difficult. As a rule such eyes, after extraction, fill up again within twenty-four hours of their own accord. But loss of vitreous may also be due to adhesion of the lens to the anterior hyaloid membrane. In 2 of my cases, during the extraction a delicate strand of vitreous became visible, which was severed in good time by the assistant and did not lead to any loss.

When in a case of cataract after cyclitis a pupillary membrane exists, the synechias should be detached as usual through a peripheral or a total iridectomy and the lens extracted behind the pupillary membrane. When vitreous does not press forward after the extraction of the lens, one can sever the pupillary membrane and the attached iris at 6 o'clock with deWecker scissors immediately after the extraction of the lens. If the vitreous presses forward into the anterior chamber, one should finish the cataract extraction and undertake iridectomy several weeks later, as otherwise the limiting membrane of the vitreous may easily be incised and vitreous thereby lost.

Nevertheless, the benefit of the intracapsular cataract extraction in such severely damaged eyes is so great that this method, first applied systematically by A. Knapp, marks an important advance in the progress of operative ophthalmology. Poor vision after cataract extraction in eyes with previous iritis or glaucoma is due to opacity of the vitreous, choroiditis, glaucomatous optic nerve atrophy or other complications of the fundus.

## EXPERIMENTAL STUDIES ON THE VITREOUS

### I. Experiments on Diffusion in the Vitreous and on Permeability of Its Surface Condensation Layer

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CLINICAL experience and scattered experimental data indicate that diffusion in the vitreous is slow.<sup>1</sup> These observations were confirmed in systematic studies of Fischer<sup>2</sup> on diffusion of hemoglobin in arbitrarily divided samples of vitreous and in examinations on spreading of penicillin after intravitreal injection in the living eye.<sup>3</sup> New information on this subject was gained by Kinsey, Grant and Cogan<sup>4</sup> in determining the total movement of vitreous water, with deuterium oxide (heavy water; D<sub>2</sub>O) as a tracer substance. The authors concluded from their experiments that the movement of water in the rabbit vitreous was of a magnitude of about 85 cu. mm. per minute. Studies on the eye with radioactive sodium (Na<sup>24</sup>) autographs<sup>5</sup> provided instructive photographic imprints on diffusion of this normal body constituent in rabbit eyes under physiologic conditions. It was distributed homogeneously throughout the vitreous two to four hours after intraperitoneal injection. The comparison of radio-

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1. Schöler, H.: Ueber das Fluorescein in seiner Bedeutung für die Erforschung des Flüssigkeits-Wechsels im Auge, Verhandlungen der physiologischen Gesellschaft zu Berlin, (February 1882), Arch. f. Anat. u. Physiol., 1882, p. 120. Schöler, H., and Uhthoff, W.: Das Fluorescein in seiner Bedeutung für den Flüssigkeits-Wechsel des Auges, in Schöler, H.: Jahresberichte der (früher Ewers'schen) Augen-Klinik, Berlin, H. Peters, 1881; abstracted, Jahresb. ü. d. Leistung. d. Ophth. **13**:91, 1882. Hamburger, C.: Ueber die Ernährung des Auges, Leipzig, Georg Thieme, 1914.

2. Fischer, F. P.: Ueber die Diffusion von Hämoglobin gegen Kammerwasser, Glaskörper und Blutserum, Arch. f. Augenh. **105**: 431-442, 1932.

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graphs obtained from eyes in which radioactive sodium was introduced topically intra vitam or after enucleation gave supporting evidence of a through and through circulation in the animal's vitreous. Radioautographs developed after systemic use of radioactive iodine ( $I^{131}$ )<sup>6</sup> showed that physical factors other than simple diffusion must be considered in the distribution of sodium iodide in the vitreous. In the experiments reported here, attempts were made to investigate the diffusion of hemoglobin and also of weak and strong acids and bases in the vitreous under various conditions without destroying or disorganizing its architectural structure, and to study the permeability of the condensation layer of the vitreous surface with the same test substances.

### DIFFUSION OF HEMOGLOBIN IN THE VITREOUS TECHNIC

Great care was exercised to avoid or minimize destruction or disarrangement of boundary membranes by applying to fresh pig and steer eyes a technic which was described in a previous paper on the  $p_H$  volume curve of the vitreous body.<sup>7</sup> The base of the vitreous and the area Martegiani were protected by leaving the ciliary body and nerve head in place. A ring of sclera and cornea 3 mm. in width supported the preparations when they were suspended in glass jars filled with an isotonic solution of sodium chloride variously buffered to desired  $p_H$  ranges. A crystal of thymol was added to the outside fluid to reduce bacterial growth. Thus, the uninjured condensation layer of the vitreous surface was exposed in large windows of the covering coats. Through the openings one could directly observe the movement of hemoglobin, which had been injected with a fine needle (27 gage) either axially or into the more densely packed peripheral region of the vitreous. The solutions of homologous hemoglobin were prepared according to the technic of Fischer.<sup>2</sup> He mixed 2 cc. of 5 per cent sodium citrate with 9 cc. of fresh blood. The red blood cells were centrifuged and resuspended in a 0.9 per cent solution of sodium chloride and again centrifuged. The washing was repeated three times. The washed cells were hemolyzed in distilled water, and the ghosts were removed by centrifugation. The hemoglobin content of the solution was determined in a Sahli hematometer. Pig hemoglobin was used in a 40 per cent concentration; steer hemoglobin, in a 60 per cent concentration. Amounts of 0.1 and 0.15 cc., respectively, were injected into the individual preparations. In experiments on the effect of temperature, groups of 4 to 10 preparations were kept in the refrigerator at 6 C., at room temperature or in the incubator at 37 C. Spreading of hemoglobin either was estimated in fractions of vitreous volume or was determined in linear measure by projecting a millimeter scale at the diffusion zone of the hemoglobin at standard time intervals. Modifications of the technic in other series of experiments will be described in the text.

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6. von Sallmann, L., and Dillon, B.: Studies of the Eye with Radioiodine Autographs, read at a meeting of Association for Research in Ophthalmology in Philadelphia, June 1949, *Am. J. Ophth.*, to be published.

7. von Sallman, L.: Expansion Tendency of the Vitreous and Its  $p_H$  Volume Curve, *Arch. Ophth.* 25: 243-254 (Feb.) 1941.

EFFECT OF TEMPERATURE AND AUTOLYSIS ON  
DIFFUSION OF HEMOGLOBIN

*Pig Vitreous.*—At the start the injected hemoglobin was confined to a small spherical or ovoid area. The depot did not change its size for the first six hours, irrespective of the temperature to which the preparations were exposed. At refrigerator temperature the test substance had diffused within eighteen hours into a portion which was estimated to be about one third or less of the vitreous volume. At a temperature of 37 C., the spreading of hemoglobin involved after eighteen hours at least two thirds of the vitreous, or the entire preparation was stained homogeneously. The results on the specimens kept at room temperature lay about midway between those recorded

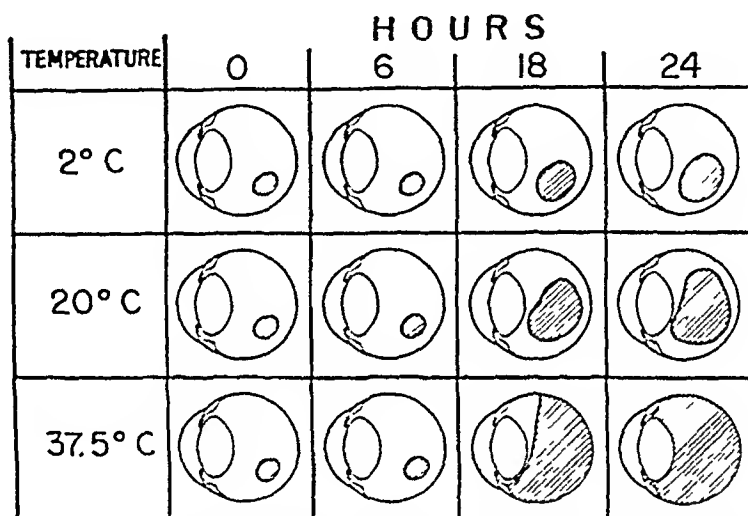


Fig. 1.—Diffusion of hemoglobin in fresh pig vitreous. Shaded areas represent inhibition of vitreous with hemoglobin.

at the two extremes of temperature. Six hours later the stained area was increased to about 60 per cent of the vitreous volume at 6 C., whereas diffusion was complete throughout the colloidal system at the higher temperature ranges. At the forty-eight hour interval autolytic liquefaction of the vitreous was so advanced in preparations kept at 37 C. that this group was discarded. The difference in extent of diffusion between the two remaining groups was still noticeable, as at 6 C. imbibition of the vitreous by hemoglobin was limited to about two thirds of the preparation. In this series the placing of the hemoglobin depot in the looser central portion or in a denser peripheral area of the vitreous did not seem to influence the diffusion gradient. No adsorption phenomena were noticed in the interphases between the fibrillar framework and the liquid content in any of these experiments, which were carried out at a neutral  $p_H$  of the outside fluid.

In another series, 36 fresh pig eyes were stored for twenty-four hours at room temperature to induce partial autolysis before injection of the hemoglobin solution. Because pig eyes can be prepared satisfactorily with the described technic only when they are fresh, the hemoglobin was introduced into the intact globes. As in previous experiments, the eyes, in groups of 6, were kept at the three temperature levels for periods of six and eighteen hours. At the termination of the experiment the globes were frozen in a freezing mixture and dissected. At the end of the six hour period the diffusion of the hemoglobin was advanced in all three groups, although at the low tempera-

TABLE 1.—*Effect of Temperature on Diffusion of Hemoglobin in Fresh Steer Vitreous*

Temperature, Degrees (C.)	Number of Prepara- tions	Average Reading, Mm. at					
		0.5	1	2	3	6	20 Hours
6	12	0.9	1.3	1.6	2.0	3.0	5.3
28	12	1.1	1.8	2.5	2.6	3.6	7.6
37	12	1.5	2.1	2.8	3.1	4.9	7.9

ture it did not exceed one-half the vitreous volume. Eighteen hours after injection the hemoglobin had diffused throughout the vitreous in all instances. The difference in the three groups observed at this interval in the previous series was abolished.

TABLE 2.—*Effect of Temperature on Diffusion of Hemoglobin in Partly Autolyzed Steer Vitreous*

Temperature, Degrees (C.)	Number of Preparations	Average Reading, Mm. at					
		1	2	3	4	6	20 Hours
6	11	1.6	2.2	2.8	3.2	4.4	6.8
37	12	1.7	2.4	3.0	3.6	5.1	7.4

*Steer Vitreous.*—Steer vitreous, with its high turgidity, lent itself better to measurements which could be expressed in millimeters per time unit, as shown in tables 1 and 2. The movement of hemoglobin was considerably slower than in the vitreous of pigs, but a diffusion zone of 1 to 2 mm. was observed as early as thirty minutes after injection at all temperature levels. Since the hemoglobin solution was not made isotonic prior to injection, it must be assumed that osmotic forces were responsible for the early spreading. An alternative explanation may be sought in the pressure produced by displaced constituents of the turgid medium. Measurements were then repeated at hourly intervals. Generally the results were in accordance with those described for pig eyes. The zone of diffusion in the preparations kept at 37 C.

was about 1.5 to 1.6 times that measured in vitreous kept at 6 C. The amount of spreading was less consistent in experiments at room temperature, because the latter varied greatly in the summer months.

Partly autolyzed vitreous of steer eyes could be prepared with the technic used for fresh eyes (table 2). The eyes had been kept at room temperature for twenty-four hours before the experiments started. It can be seen in figure 2 that the difference in speed of diffusion under the influence of increments of temperature was strikingly less. As in experiments on pig vitreous, no adsorption phenomena on intra-

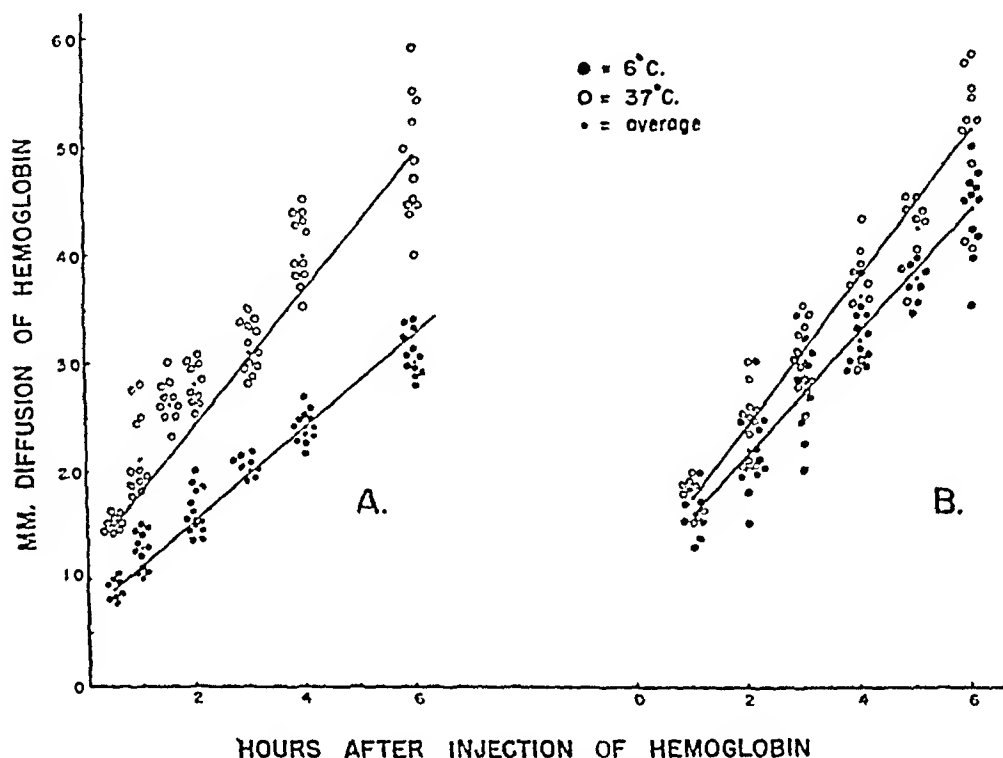


Fig. 2.—Diffusion of hemoglobin in steer vitreous at 6 and 37 C.: (A) fresh preparations; (B) partly autolyzed preparations.

vitreal phase boundaries were encountered. When hemoglobin was accidentally placed in the hyaloid canal, it filled this potential axial space. Such preparations were excluded from the experiments.

#### EFFECT OF HYDROGEN ION CONCENTRATION ON DIFFUSION OF HEMOGLOBIN IN STEER VITREOUS

Groups of vitreous preparations like those used in the former series were suspended for twenty-four hours in isotonic solution, buffered to a pH of 4, 6, 7 and 8. The relatively rapid permeation of hydrogen and hydroxyl ions into the vitreous from the outside fluid was demonstrated in experiments, which will be discussed later. The hydrogen ion concentration of the outside fluid was measured at the end of the experiment and for all practical purposes was found unchanged when

compared with the original values (table 3). The preparations were stored in the refrigerator at 6 C. At  $p_H$  4 the diffusion rate was

TABLE 3.—*Effect of Hydrogen Ion Concentration on Diffusion of Hemoglobin in Steer Vitreous\**

$p_H$	Number of Preparations	Average Reading, Mm. at			
		1	2	6	18 Hours
4	4	1.6	2.0	3.4	6.9
6	4	1.3	1.8	2.8	5.8
7	4	1.3	1.7	2.8	5.9
8	4	1.4	1.8	2.6	5.8

\* Preparations were kept at 6 C.

increased 0.1 to 0.25 time over that obtained in the control experiments at a neutral  $p_H$  (fig. 3). Differences of the diffusion zones at  $p_H$  6

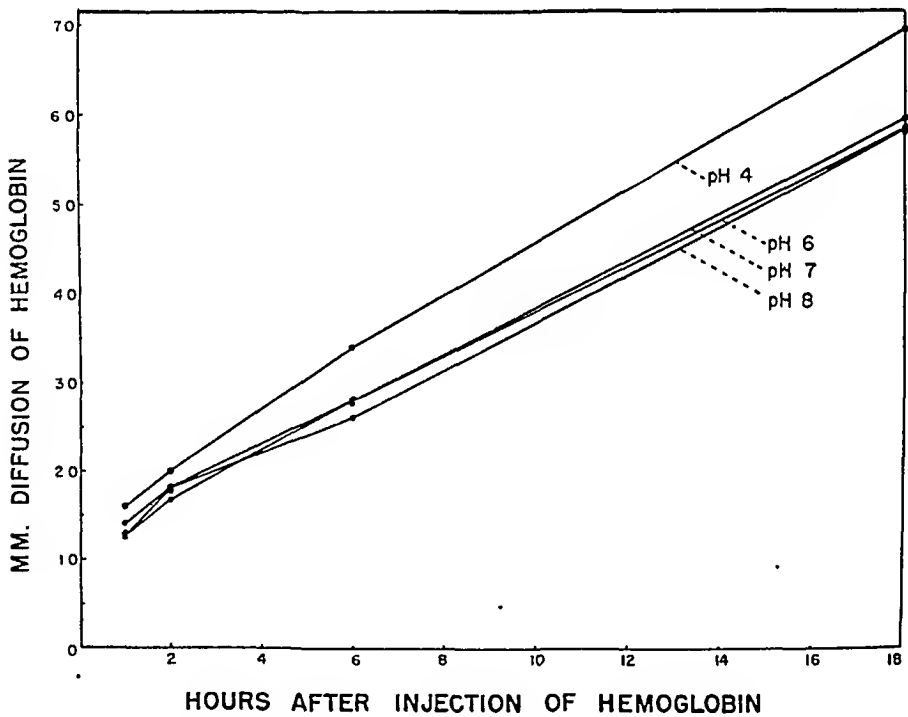


Fig. 3.—Diffusion of hemoglobin in steer vitreous at  $p_H$  levels of 4, 6, 7 and 8.

and 8 and at  $p_H$  7 were not significant. No depositions of hemoglobin were seen macroscopically at any of the  $p_H$  levels studied.

#### EFFECT OF THE ENZYME HYALURONIDASE ON DIFFUSION OF HEMOGLOBIN AND NIAGARA BLUE IN FRESH STEER VITREOUS: TENTATIVE EXPERIMENTS

*Observations.*—With a technic resembling that employed in other series, 60 per cent hemoglobin was injected in 6 vitreous preparations of steer eyes. In 3 preparations hyaluronidase was incorporated in

the hemoglobin solution so that the injected mixture contained 100 depolymerizing units of the enzyme.<sup>8</sup> The preparations were suspended in an isotonic solution of sodium chloride which was buffered to a  $p_H$  of 7. Temperatures of 6 and 37 C. were used. In the observation time of twenty-four hours no difference in extent of diffusion was observed between the preparations with the enzyme and the controls.

In a second series, of 12 preparations, a 1 per cent solution of Niagara blue (pontamine sky blue) was used instead of hemoglobin. The experiments were carried out at the three temperature levels, 6, 25 to 30, and 37 C. At refrigerator and room temperatures the preparations with the enzyme showed in a five hour period the same diffusion as the controls. At the incubator temperature (37 C.) small amounts of the dye had diffused partially into the surrounding fluid three and one-half hours after injection of the dye-enzyme mixture, whereas it had not passed the surface membrane of the controls.

*Comment.*—The effect of temperature on diffusion of homologous hemoglobin in grossly undisturbed fresh preparations of vitreous was in the less turgent pig vitreous greater than in steer vitreous under the same experimental conditions. Although the measurements in the latter were more accurate, they could not be subjected to mathematical analysis. The difference in the vitreous of two species (pig and steer) and the difference in the speed of diffusion between fresh and partly autolyzed preparations pointed to the importance of the structural state of the medium in which the movement of hemoglobin was estimated.

Krause<sup>9</sup> assumed that autolytic disintegration of the vitreous involves, first, peptones, albumins, globulins and the sulfur-containing glucoprotein (mucoid) which was described by Levene.<sup>10</sup> Since this compound was characterized by its gelatinous nature, decrease in turgescence in early stages of autolysis could, according to Krause, be due to the breakdown of the mucoid. Autolytic hydrolysis of the structural proteins seems to follow at a later stage. Meyer and Palmer<sup>11</sup> isolated from the vitreous a sulfur-free, viscous mucopoly-saccharide, which they called hyaluronic acid. The authors concluded

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8. A potent preparation of hyaluronidase prepared from bull testes was supplied from the laboratory of Dr. Karl Meyer.

9. Krause, A. C.: *The Biochemistry of the Eye*, Baltimore, Johns Hopkins Press, 1934, p. 176; Wilmer Ophthalmological Institute, Johns Hopkins Hospital and University, Monograph no. 2.

10. Levene, P. A.: *Hexosamine and Mucoproteins in Monographs on Biochemistry*, London, Longmans, Green & Co., 1925.

11. Meyer, K., and Palmer, J. W.: *On Glycoproteins: II. The Polysaccharides of Vitreous Humor and of Umbilical Cord*, J. Biol. Chem. **114**: 689-703 (July) 1936.

that this compound was responsible for the turgor and viscosity of the vitreous. The discrepancy between the data of Levene and those of Meyer and Palmer was discussed by the latter authors.<sup>11</sup> In autolysis, depolymerization of hyaluronic acid to a nonviscous form could possibly be brought about by liberation or activation of hyaluronidase from neighboring tissues. The breakdown of the acid might influence liquefaction of the fibrillar network of the vitreous, which is presumably composed of the structural proteins. Recent investigations of Pirie<sup>12</sup> indicated that aggregated hyaluronic acid, as contained in the vitreous jelly, interacts with the structure of the insoluble protein. She concluded from her experiments that "liquefaction of the insoluble proteins was slowed by the presence of the aggregated hyaluronic acid and disaggregation of hyaluronic acid was slowed down by the presence of the insoluble protein." The sequence of changes has not been studied in autolytic liquefaction of the vitreous.

Decrease of viscosity obviously caused in autolyzed preparations more rapid diffusion of hemoglobin. Reduction of frictional forces could be attributed as well to the change of highly polymerized hyaluronic acid to a nonviscous state as to the change in filtering action and adsorption factors which are supposedly functions of the fibrillar structures of the vitreous. However, the diffusion experiments in which the mucolytic enzyme hyaluronidase was added to hemoglobin or dye-stuff showed that the jelly of hyaluronic acid was not noticeably liquefied by the enzyme. Similar observations were reported by Blix<sup>13</sup> and by Pirie.<sup>12</sup> These authors did not notice any liquefaction of fresh steer vitreous after use of hyaluronidase. The only exception to the rule in the present experiment was the behavior of Niagara blue in the dye-enzyme mixture at incubator temperature. It seems unlikely, therefore, that depolymerization of hyaluronic acid plays an important part in the initial decrease of viscosity in partially autolyzed vitreous of pig and steer eyes.

The isoelectric point of hemoglobin is at  $p_H$  6.8 to 7. Changes in the  $p_H$  of the surrounding fluid to 4, 6 and 8 did not noticeably alter the smooth slope of the diffusion gradient when examined macroscopically and did not lead to macroscopically visible adsorption. One would expect that the ionization and hydration of the hemoglobin molecule at an acid  $p_H$  of 4 would produce a decrease in diffusion rate, rather than the increase which was observed in the experiments. It is possible that the diminution in friction of the hydrated molecules or reversible denaturation of the hemoglobin molecule overcompensated

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12. Pirie, A.: Ox Vitreous Humor: II. Hyaluronic Acid Relationships, *Brit. J. Ophth.* **33**: 271-283 (May) 1949.

13. Blix, G.: Some Aspects of the Physiology and Pathology of the Natural Hexosamine and Uronic Acid Compounds, *Biochem. J.* **40**: 6-7, 1946.

the effect produced by the increase in size due to hydration. The acidity in the vitreous in acute experimental infections did not exceed a  $p_H$  of 5.7,<sup>14</sup> so that the rise in the diffusion rate for large molecules in a stronger acid range ( $p_H$  4) has no direct practical applicability.

It is not feasible to compare the data obtained with other test substances (deuterium oxide, radioactive sodium) with those obtained with hemoglobin because the former experiments were carried out on vitreous of low consistency (rabbit). However, among other factors, dependence of the diffusion rate on the molecular size of the used compound cannot be doubted. It was substantiated in the reported experimental series by the speedier movement of Niagara blue as compared with that of hemoglobin in steer vitreous.

#### EXPERIMENTS ON PERMEABILITY OF THE SURFACE CONDENSATION LAYER OF STEER VITREOUS PERMEABILITY TO HEMOGLOBIN

Changes in the permeability of the surface membrane of the vitreous have been considered in explaining the mechanism of some forms of secondary glaucoma. The clear therapeutic effect of Chandler's needling operation<sup>15</sup> on the vitreous membrane in certain types of glaucoma in aphakic eyes called immediate attention to disturbances in physical qualities of the surface layer which normally separates the vitreous from the posterior chamber and lens. The following experiments were designed to study the permeability of this structure to the large protein molecule.

*Technic:* Homologous hemoglobin was mixed with the isotonic solution of sodium chloride in which the vitreous preparations were suspended. A concentration of 0.2 per cent solution was used; the  $p_H$  of the solution was buffered to 7. In this series, of 11 preparations, the nerve head and ciliary body were not preserved. In 5 experiments parts of the superficial layers of the vitreous were removed in circumscribed areas. The preparations were placed in the refrigerator, and readings were taken after five, eighteen and twenty-four hours. Finally, after macroscopic inspection, the specimens were frozen in a freezing mixture and bisected. In a second series, of 10 vitreous preparations, a 60 per cent solution of hemoglobin was injected into the vitreous close to its surface to study the penetration from inside outward.

*Results.*—In the first series of experiments native and frozen preparations showed that hemoglobin penetrated the surface layer of the cortex of the vitreous, but the outermost cover of this layer was macroscopically and biomicroscopically more intensely stained. When, in

14. von Sallmann, L.: Hydrogen Ion Concentration of the Vitreous in the Living Eye, *Arch. Ophth.* **33**: 32-39 (Jan.) 1945.

15. Chandler, P. A., and Johnson, C. C.: A Neglected Cause of Secondary Glaucoma in Eyes in Which the Lens Is Absent or Subluxated, *Arch. Ophth.* **37**: 740-771 (June) 1947.



several instances, the posterior capsule of the lens had remained on the anterior face of the vitreous preparation, it also took up more of the hemoglobin. On the other hand, the area Martegiani and arbitrarily produced defects of the superficial layer showed much less tinction by the coloring matter. Penetration of hemoglobin from the environment into the vitreous substrate extended to a depth of 7 mm. in a twenty-four hour period. In the second series, in preparations kept at refrigerator temperature hemoglobin did not penetrate the surface condensation layer from within for ten hours. The otherwise spherical outline of the diffusion zone was flattened at the surface, corresponding to the contour of the outermost layer. In preparations kept at 37 C. hemoglobin was not completely retained by the condensation membrane at the ten hour interval. A very moderate diffusion through the membrane was noticed even as early as three and one-half hours after injection.

*Comment.*—The experimental results indicated that the surface layer of the vitreous trapped the large molecule of hemoglobin and offered increased frictional resistance to the passing of hemoglobin inward and outward. These observations suggest that the outer boundary of the vitreous is the seat of a characteristic permeability and that it may be thought of as a semipermeable membrane. This permeability differs from that of the enclosed system and its interphases; here the permeability for hemoglobin was equal throughout, as shown in previous experiments. It is known that physical changes of surface membranes, such as stretching or contraction, can alter their permeability. Such mechanical forces may have been active at the low temperature of the refrigerator and may have added to the effect of the relatively high frictional resistance apparently located in the densely packed mesh of the fibrils of the surface layer. A distinct difference in the behavior of the outer boundary of the vitreous as compared with its bulk was observed by Redslob<sup>16</sup> by treating isolated vitreous preparations with a 5 per cent solution of pyridine. Only the intact surface layer developed a gray opacity. A similar change could be produced with pyridine in dissected human eyes with detachment of the vitreous.<sup>17</sup>

#### PERMEABILITY TO STRONG AND WEAK ACIDS AND BASES

The penetration of hydrogen and hydroxyl ions into a colloidal system is of great interest. Many studies have been conducted to investigate the relative penetrating power of these ions on plant cells (*Elodea*,<sup>18</sup>

16. Redslob, E.: *Le corps vitré, son développement, sa structure, ses propriétés physicochimiques*, Paris, Masson & Cie, 1932.

17. von Sallmann, L.: *Zur Anatomie der hinteren Glaskörperabhebung*, Arch. f. Ophth. **135**: 593-601, 1936.

18. Harvey, E. N.: *Studies on the Permeability of Cells*, J. Exper. Zool. **10**: 507-556, 1911.

Spirogyra,<sup>19</sup> Valonia,<sup>20</sup> Nitella,<sup>21</sup> cells of flowers of Rhododendron<sup>22</sup>) and animal cells (Arbacia eggs,<sup>23</sup> starfish eggs,<sup>21b</sup> red blood corpuscles<sup>24</sup>). The technic applied in some of these studies could be modified for use in vitreous preparations.

*Technic.*—A small amount (0.15 cc.) of an indicator was injected with a fine needle into the central area of isolated preparations of vitreous of steer eyes. A solution of bromthymol blue in a 0.04 per cent concentration or of phenolsulfonphthalein U. S. P. in a 0.02 per cent concentration was used. The solution formed at the start a circumscribed colored area, from which it diffused within a few hours in all directions within the specimen. The preparations were then suspended in about 400 cc. of a 1/400 molar solution of a strong acid or base, i. e., hydrochloric acid and sodium hydroxide, or in solutions of a weak acid or base, namely, acetic acid and ammonium hydroxide. The preparations were kept at 6 C. and observed for six to twelve hours. The speed of penetration was estimated by plotting time against distance measured from the zone where the change in color occurred to the surface of the specimen. Intact vitreous preparations and preparations with arbitrarily produced injuries of the surface layers were compared. Observations were made on 44 vitreous preparations. In an additional series, 16 preparations were first placed at 6 C. in homologous serum for twelve hours and then suspended in the solutions of acids or bases. Fourteen preparations kept in a 0.9 per cent buffered solution of sodium chloride were stored for the same length of time in the refrigerator prior to the transfer of the specimen into the test solutions to serve as controls.

*Normal and Injured Vitreous Preparations.*—Hydrochloric acid diffused more rapidly than sodium hydroxide. Acetic acid penetrated at a faster rate than ammonium hydroxide. The movement of the weak acid exceeded that of the strong one. The same relation was observed

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19. Harvey, E. N.: Relation Between the Rate of Penetration of Marine Tissues by Alkali and the Change in Functional Activity Induced by the Alkali, Washington, D. C., Carnegie Institute, publication no. 183, 1914, vol. 6, pp. 131-146.

20. Brooks, M. M.: Studies on the Permeability of Living and Dead Cells: I. New Quantitative Observations on the Penetration of Acids into Living and Dead Cells, United States Pub. Health Rep. 38: 1449-1470, 1923; III. The Penetration of Certain Alkalis and Ammonium Salts into Living and Dead Cells, *ibid.* 38:2074-2086, 1923.

21. (a) Hoagland, D. R., and Davis, A. R.: Further Experiments on the Absorption of Ions by Plants, Including Observations on the Effect of Light, J. Gen. Physiol. 6: 47-62, 1923. (b) McCutcheon, M., and Lucké, B.: The Mechanism of Vital Staining with Basic Dyes, *ibid.* 6: 501-507, 1924. (c) Irwin, M.: Accumulation of Brilliant Cresyl Blue in the Sap of Living Cells of Nitella in the Presence of NH<sub>3</sub>, *ibid.* 9: 235-253, 1925.

22. Jacobs, M. H.: The Influence of Ammonium Salts on Cell Reaction, J. Gen. Physiol. 5: 181-188, 1922.

23. Warburg, O.: Ueber die Oxydationen in lebenden Zellen nach Versuchen am Seeigellei, Ztschr. f. physiol. Chem. 66:305-340, 1910. Stewart, D. R.: The Permeability of the Arbacia Egg to Ammonium Salts, Biol. Bull. 60: 171-178, 1931.

24. Jacobs, M. H.: The Permeability of Erythrocytes, Ergebn. Biol. 7: 1-55, 1931. Jacobs, M. H., and Parpart, A. K.: Is the Erythrocyte Permeable to Hydrogen Ions? Biol. Bull. 62: 63-73, 1932.

between equimolar solutions of sodium and ammonium hydroxide. Injuries to the surface layers of the vitreous suggested in several instances an increase in penetration rate, but in other preparations no difference was observed between intact and injured parts of the surface.

*Preparations Pretreated with Homologous Serum.*—The impregnation of the marginal layers of the vitreous with serum protein slowed

TABLE 4.—*Diffusion of a Strong and Weak Acid and a Strong and Weak Base into Fresh Steer Vitreous Suspended in 1/400 Molar Solutions*

Number of Preparations	Acid or Base	Average Reading, Mm. at			
		1	2	3	4 Hours
A. Intact Preparations					
12*	Sodium hydroxide	2	4	6	12
7	Ammonium hydroxide	4	8	10	14
11*	Hydrochloric acid	4	6	11	14
6	Acetic acid	5.5	9	10	15
B. Injured Preparations					
4	Sodium hydroxide	2	5	7	11
4	Hydrochloric acid	5	8	14	15

\* Including 4 preparations which served as controls in B.

down the diffusion of  $H^+$  from both types of acids. The rate of penetration of bases was less affected by the accumulation of the proteins in the surface zone of the preparation.

*Comment.*—The more rapid penetration of hydrogen ions through the surface membrane and the speedier diffusion in intact vitreous preparations as compared with hydroxyl ions may have their cause in

TABLE 5.—*Diffusion of Acid and Base into Serum-Soaked Preparations of Steer Vitreous Suspended in 1/400 Molar Solutions*

Number of Preparations	Acid or Base	Average Reading, Mm. at			
		1	2	3	4 Hours
Experimental 4	Sodium hydroxide	3	5	7	10
Controls 3	Sodium hydroxide	3	6	9	14
Experimental 4	Ammonium hydroxide	4	6	9	12
Controls 3	Ammonium hydroxide	5	8	12	15
Experimental 4	Hydrochloric acid	3	5	8	10
Controls 4	Hydrochloric acid	6	11	15	..
Experimental 4	Acetic acid	4	6	9	11
Controls 4	Acetic acid	6	11	15	..

the smaller size of the former or in differences in changes in the diffusion medium produced by acids and bases. Molecules have the property of penetrating colloidal systems relatively faster than ions. The rate of penetration depends, therefore, on the dissociation constant of the substance studied. As in experiments on plant cells and animal cells, weak acids and bases entered the vitreous at a faster rate. Rapid diffusion of  $NH_4$  and the subsequent change in the  $pH$  in the steer vitreous were in agreement with numerous observations made in experimental biology.

Results in preparations of normal vitreous with injured surface layers suggested in the majority of experiments a moderate increase of penetrability for the acids and bases used, but this observation was not confirmed in other instances. In these experiments it was not possible, therefore, to demonstrate an unquestionable difference in the permeability between the outer boundary and the enclosed system as it was indicated in the studies with hemoglobin. The impregnation of peripheral layers of the vitreous with serum proteins delayed the onset of the changes in the  $pH$  in the more central portion of the vitreous. The most likely explanation of this phenomenon may be seen in increase of buffering capacity in the surface zone of the vitreous due to accumulation of serum protein. Blocking of the pore system of the membrane sieve with increased frictional resistance represents another mechanism which must be considered. The surface layers of the preparation which had been pretreated with serum developed in the acid environment a gray, dense precipitation film. This physicochemical change may have impeded the movement of the test substances in later stages of the experiment.

#### SUMMARY

1. The diffusion rate of homologous hemoglobin in undamaged vitreous preparations was increased by temperature increments and by autolytic decomposition of the colloidal system. These influences were greater in pig than in steer vitreous.

2. In general, mixtures of hemoglobin or Niagara blue with hyaluronidase preparations did not diffuse more rapidly in steer vitreous than did hemoglobin or the dye alone.

3. At  $pH$  ranges of from 6 to 8 changes in the hydrogen ion concentration of the milieu did not noticeably influence the character or rate of diffusion of hemoglobin in the steer vitreous.

4. The surface condensation layer of the vitreous differs in its permeability for hemoglobin from the permeability of the enclosed system and its boundary interphases.

5. Hydrochloric acid penetrated the surface layer and diffused at a higher rate in the vitreous than did sodium hydroxide. Similarly, acetic acid moved faster than ammonium hydroxide. The diffusion rate of the weak acid and base exceeded that of the strong acid and base.

6. No distinct difference in permeability for hydrogen ions and hydroxyl ions was demonstrated between the surface membrane and the bulk of the vitreous body.

7. Impregnation of the peripheral vitreous layers with serum proteins slowed the penetration of acids and, to a lesser degree, that of bases.

Dr. Karl Meyer supplied me with the enzyme preparations. Miss J. Di Grandi and Miss B. Dillon assisted in this study.

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## CATARACT FORMATION IN THE HUMAN EMBRYO AFTER RUBELLA

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**B**ILATERAL cataract formation in an 11 week embryo with a history of rubella in the mother during the eighth week of pregnancy is of sufficient interest to warrant publication.

Reese<sup>1</sup> (1944) recorded the first observation in the United States of congenital cataract formation in infants born of mothers who had rubella in the early part of pregnancy. The original description of this condition was made by Gregg<sup>2</sup> and by Swan and his co-workers.<sup>3</sup> An epidemic of rubella in Australia aroused their attention to the prevalence of this condition. Since the aforementioned reports, many cases have been recorded, so that the process is now well recognized. Besides cataract formation, the infants have other defects: intolerance to atropine; inability to dilate the pupil; a high incidence of susceptibility to pneumonia, with high fever; mental deficiency, and microcephaly. Deaf-mutism has also been reported fairly frequently. The children are small, ill nourished and difficult to feed.

The cataractous lens shows involvement of all but the outermost layers, and the cataract is considered to have developed early in embryonic life. Though the condition is usually bilateral, monocular involvement has been reported. Nystagmus, strabismus, corneal opacities, microphthalmos and glaucoma have also been observed.

Since publication of the studies by Swan and Tostevin,<sup>4</sup> the first three months are conceded to be the critical period of pregnancy for the development of congenital abnormalities resulting from rubella.

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From the Francis I. Proctor Foundation for Research, Division of Ophthalmology of the University of California.

1. Reese, A. B.: Congenital Cataract and Other Anomalies Following German Measles in the Mother, *Am. J. Ophth.* **27**:483 (May) 1944.

2. Gregg, N. M.: Congenital Cataract Following German Measles in Mother, *Tr. Ophth. Soc. Australia* **3**:35, 1942.

3. Swan, C.; Tostevin, A. L.; Moore, B.; Mayo, H., and Black, G. H. B.: Congenital Defects in Infants Following Infectious Diseases During Pregnancy, *M. J. Australia* **2**:201 (Sept.) 1943.

4. Swan, C., and Tostevin, A. L.: Congenital Abnormalities in Infants Following Infectious Diseases During Pregnancy, with Special Reference to Rubella: A Third Series of Cases, *M. J. Australia* **1**:645 (May) 1946.

So far as involvement of the lens is concerned, this has been verified, since no cases of cataract have been reported in which rubella was contracted after the third month. Substantiation of the belief that changes do occur in the lens during the first trimester has been very limited. The number of embryos obtained for study from women having rubella during the first trimester has been very small.

Swan<sup>5</sup> described the first embryo in 1944. A 2½ month embryo was obtained from a woman who had had rubella late in the second month of pregnancy. Examination disclosed considerable disorganization of the structures of the right eye, including microphthalmos, cataract formation and failure of closure of the fetal fissure. The blood vessels supplying the lens were reduced in number. The left eye failed to show any abnormality. In this embryo, then, there were definite abnormalities, which included actual cataract formation in one eye, while the other eye was normal. This occurrence coincides with clinical observations that in some children cataract formation may develop in only one eye.

The second case was reported by Cordes and Barber<sup>6</sup> in 1946. The specimen consisted of an embryonic eye recovered after a therapeutic abortion, terminating a pregnancy of eight weeks. There was a history of rubella in the mother during the fifth week. Microscopic examination revealed that the optic cup was well formed and the outer layer fully pigmented. The outer and inner walls of the optic cup had become approximated, and the fetal fissure had closed. The hyaloid system was fully developed, and the hyaloid artery contained blood. The cells of the posterior portion of the retina had differentiated into the inner and outer neuroblastic layers. Mesodermal tissue covered the anterior surface of the lens, but the anterior chamber had not formed. The anterior portion of the tunica vasculosa lentis was poorly defined, but the lateral and posterior portions appeared normal. The subcapsular epithelium of the lens showed distortion and disorientation of the cells at the anterior pole. The primary fibers had elongated but did not completely fill the cavity of the lens vesicle. The fibers were swollen and stained poorly, appearing vacuolated at their anterior ends. The nuclei also stained unevenly. The lens capsule was difficult to trace. The lens showed definite retardation of development and differentiation, while the posterior segment was normal. Terry compared the specimen with those in the Minot Embryological Collection at Harvard University and stated that the lens showed the differentiation and size of a 17 mm.

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5. Swan, C.: Congenital Malformations in Infants Following Maternal Rubella During Pregnancy: A Review of Investigations Carried Out in South Australia, *Tr. Ophth. Soc. Australia* 4:132, 1944.

6. Cordes, F. C., and Barber, A.: Changes in Lens of Embryo After Rubella, *Arch. Ophth.* 36:135 (Aug.) 1946.

embryo, while the differentiation and over-all size of the eye corresponded to the 19 mm. stage. This retardation of the development of the lens was confirmed by Ida Mann when she saw the specimen.

In 1948 Helweg-Larsen, and Nielsen<sup>7</sup> of the University Institute for Human Genetics of Copenhagen, reported on the study of a 25 mm. embryo obtained after the mother had had rubella. The lens was underdeveloped, and the lens fibers did not fill the lens cavity and also showed fine vacuolation. They suggested that more young embryos from women who contracted rubella during pregnancy be studied, possibly with the aid of analysis of the ultraviolet absorption spectrum, to determine disturbances in the cell protein metabolism, which is influenced early by virus infections.

#### REPORT ON FOUR EMBRYOS

**SPECIMEN 1.**—In the early part of 1948, two embryonic eyes were received by us at the Proctor Laboratory of the Division of Ophthalmology of the University of California. Dr. James Harkins and Dr. Melvin Friedman, of the Permanente Foundation Hospital, Oakland, Calif., permitted us to present the results of study.

**History.**—The mother had rubella during the second month of pregnancy, and a therapeutic abortion was performed at the 11 week stage.

The head had been removed from the body and the eyes dissected from the orbit and fixed in dilute solution of formaldehyde U. S. P.

#### RIGHT EYE

**Gross Examination.**—The specimen measured 5 by 4 by 4 mm. Some tissue adhered to the cornea. The lens appeared dense white and opaque. The anterior chamber was very shallow, and the cornea was clear. The margin of the optic vesicle lay at about the equator of the lens.

**Microscopic Examination.**—The specimen appeared to be well fixed, as the epithelium of the eyelids and of the cornea was intact. The retina showed only very slight postmortem degeneration (fig. 1).

**Cornea.**—The corneal epithelium had undergone slight surface desquamation, and some of the central cells were completely missing. This may have occurred at the time of removal of the eye. Bowman's membrane (lamina elastica anterior) was not seen. The stroma had a uniform thickness and contained a large number of cells, a developmental stage characteristic of a fetus of the age of this specimen. Descemet's membrane (lamina elastica posterior) was not yet present. The endothelium was intact.

**Limbus.**—The anterior vascular network of the sclera was rudimentary, and the definitive trabecular meshwork was not present. Schlemm's canal was not seen.

**Anterior Chamber.**—The whole anterior chamber was extremely shallow, owing to the large size of the lens. The angle was rounded and filled with mesodermal tissue.

**Iris.**—The pupillary portion of the tunica vasculosa lentis was present. The mesodermal portion of the iris extended a short distance centrally along the anterior capsule, but the epithelial layers lay just anterior to the equator of the lens.

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7. Helweg-Larsen, and Nielsen, E. L.: Forändringar i fosterlinse efter rubeolae? Ugesk. f. læger, 1948, no. 49, p. 1394.

*Ciliary Body.*—There was very slight early differentiation of the corona with some folding of the epithelial layers. The stroma was poorly defined, and the ciliary muscle showed only slight differentiation.

*Choroid.*—Bruch's membrane (lamina basalis) was not present, and there were very loose layers of small blood vessels in the mesoderm of the choroidal stroma.

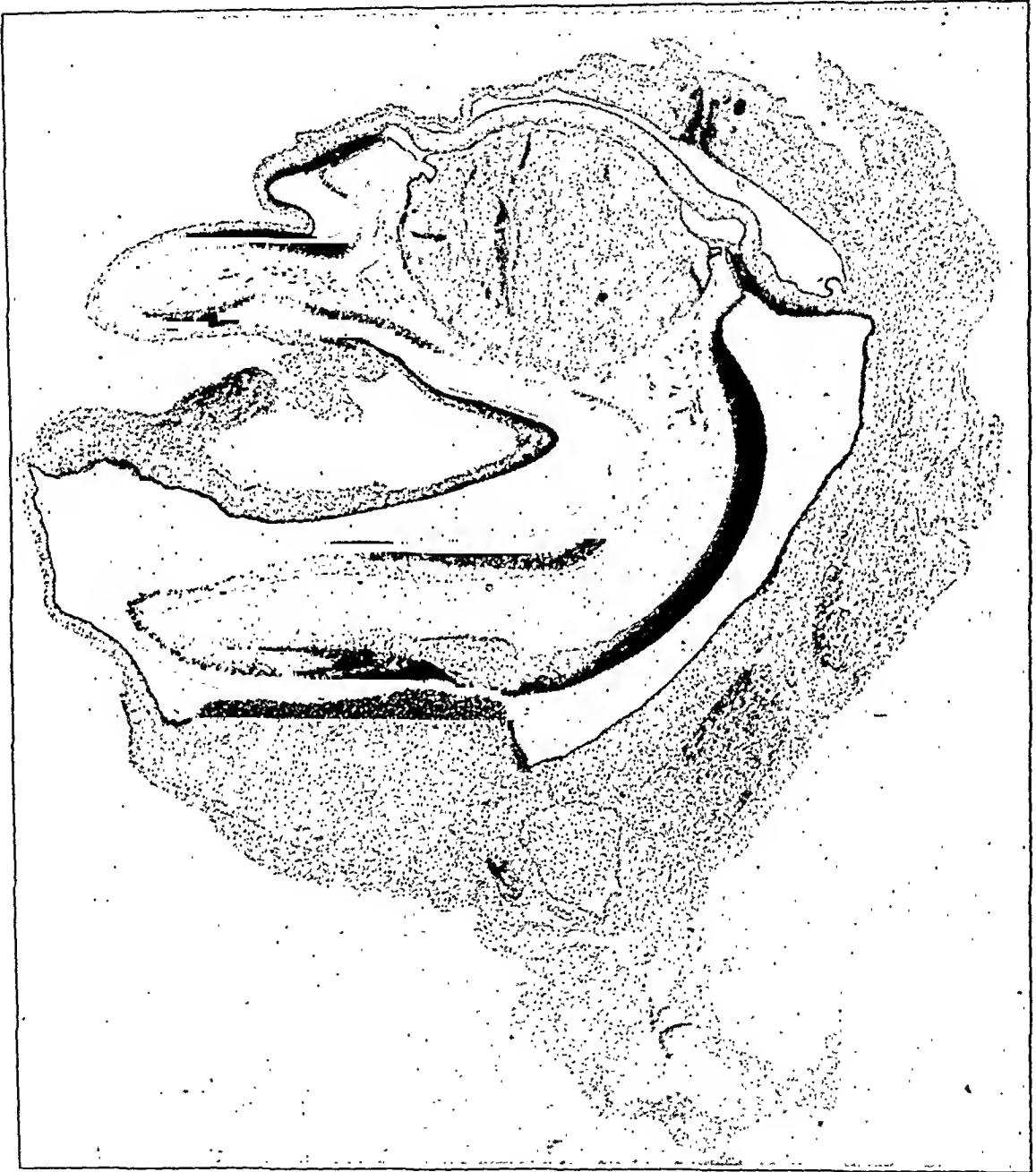


Fig. 1.—Right eye of an 11 mm. embryo ( $\times 25$ ) from a woman who contracted rubella during the second month of pregnancy, showing degeneration of primary lens fibers and early liquefactions of the secondary fibers.

*Sclera.*—The sclera was represented by a very loose mesodermal tissue on the outer surface of the choroid. Some of the extraocular muscles were seen to become confluent with this mesoderm.

*Retina.*—The retina was separated and somewhat folded, owing to shrinkage, but the nuclear and fiber layers appeared intact. The posterior portion of the



retina showed differentiation into two well defined nuclear layers, but anteriorly the differentiation was not so sharp.

*Vitreous.*—The primary vitreous occupied most of the cavity of the globe, and only a small amount of secondary vitreous was present. The vessels in the primary vitreous were filled with blood. Those of the tunica vasculosa lentis were also present and well developed.

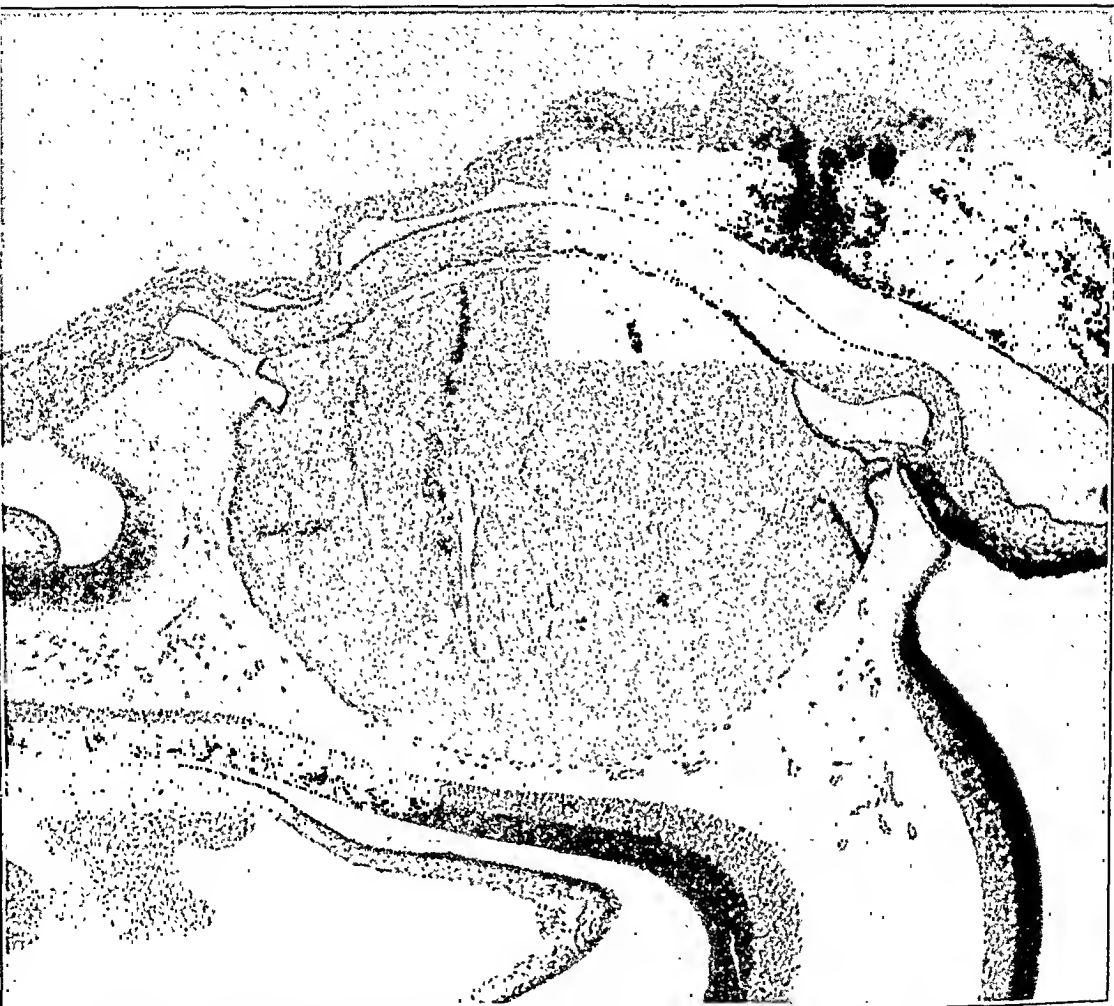


Fig. 2.—Higher magnification of the eye presented in figure 1, showing details of degenerative changes in the lens ( $\times 42$ ).

*Lens.*—The lens was rather large and rounded. The capsule was present and intact. Most of the primary and secondary lens fibers showed degeneration and liquefaction, with formation of globules and homogeneous masses of dark-staining fluid. The nuclei of the secondary lens fibers were of normal size and showed no degeneration. The nuclei of the primary lens fibers showed pyknosis and fragmentation (fig. 2).

*Diagnosis.*—The diagnosis was acquired cataract, due to rubella in the mother.

## LEFT EYE

*Gross Examination.*—The eye measured 5 by 5 by 4 cm. The cornea was clear, and there was practically no anterior chamber, owing to the large size of the lens. The lens was milky white and opaque. The sclera was thin.

*Microscopic Examination.*—The cornea, anterior chamber, iris, ciliary body, choroid, sclera, retina and vitreous resembled those structures in the right eye (fig. 3).

*Lens.*—The lens capsule was thin but intact. The anterior epithelium of the lens appeared normal. Most of the primary and secondary lens fibers showed dif-



Fig. 3.—Left eye of the 11 mm. embryo whose eye is presented in figures 1 and 2, showing extensive degeneration of both primary and secondary lens fibers ( $\times 25$ ).

fuse degeneration with formation of globules and uniform dark-straining masses of fluid. The nuclei of the secondary lens fibers were intact and appeared fairly normal, while those of the primary fibers were pyknotic and showed degeneration. The chief damage to the lens appeared to be in the primary fibers (fig. 4).

*Diagnosis.*—The diagnosis was acquired cataract, due to rubella.

Thus, the eyes of this 11 week embryo, with a history of rubella during the last part of the second month of gestation, showed cataract formation.

*Three Additional Embryos.*—During the early part of 1949, 3 additional embryos were received.

SPECIMEN 2.—A  $2\frac{1}{2}$  month embryo was received with the history that the mother had had a therapeutic abortion three weeks after a severe illness of rubella. Serial section failed to reveal cataract formation or any other abnormality of the eyes.

SPECIMEN 3.—A  $3\frac{1}{2}$  month fetus was received from another hospital with the history that two weeks before the pregnancy had been terminated the mother had a severe episode of rubella. Examination failed to show any evidence of cataract formation or other ocular anomaly.



Fig. 4.—Higher power magnification of the eye shown in figure 3, showing details of degenerative changes in the lens ( $\times 42$ ).

SPECIMEN 4.—A 3 month embryo was obtained after a therapeutic abortion a short time after a severe episode of rubella. The lenses showed no evidence of cataract formation, and the eyes seemed entirely normal.

#### COMMENT

Specimen 1 represents the second reported case in which an embryo from a mother who had had rubella during the first trimester showed cataract formation. It is the first in which both eyes were involved. This case, together with Swan's<sup>5</sup> and the case reported by Cordes

and Barber,<sup>6</sup> would bear out the contention that the damage to the lens may occur during the acute phase of rubella.

It has been observed clinically that the condition may not be bilateral. That unilaterality is determined early in the development of the embryo is exemplified in the case reported by Swan.<sup>5</sup> In his case, cataract developed in the right eye, and the left eye was normal so far as could be determined.

The consensus regarding the frequency of congenital defects following rubella during the first trimester of pregnancy has changed a great deal during the last five years. In 1944 Swan<sup>5</sup> stated that if a woman contracted rubella within the first two months of pregnancy the chances of her bearing a congenitally defective infant appeared to be in the region of 100 per cent. In 1947 Swan, Tostevin and Black<sup>8</sup> stated that it is possible that rubella in early pregnancy is not invariably followed by congenital defects in the offspring. In their combined series of cases, however, only 3 of the 62 babies whose mothers had had the infection during the first two months of pregnancy were free of congenital abnormalities. In an editorial appearing in the *British Medical Journal*<sup>9</sup> in 1946 it was stated that from the available evidence it appeared that the chance of rubella affecting the fetus if the disease was contracted by the mother during the first months of pregnancy was 10 per cent. In 1947 Aycock and Ingolls<sup>10</sup> found that, according to American statistics, defects occurred in only 25 per cent of the children whose mothers had rubella in the first three months of pregnancy. In 1947 Wesselhoeft<sup>11</sup> stated that a woman contracting rubella during pregnancy had approximately 1 chance in 10 of subsequently being delivered of a congenitally defective child. The preliminary report on the relation of various infections occurring in the first trimester of pregnancy to defects in offspring, sent out by Dr. Herbert C. Miller and his committee, has interesting figures on cataract formation. Of 89 children whose mothers had rubella during the first three months of pregnancy, 51 showed cataract formation. The highest incidence occurred in those cases in which the disease was present between the fifth and the eighth week.

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8. Swan, C.; Tostevin, A. L., and Black, G. H.: Final Observations on Congenital Defects in Infants Following Infectious Diseases During Pregnancy with Special Reference to Rubella, *M. J. Australia* **11**:889 (Dec.) 1946.

9. Rubella and Congenital Abnormalities, editorial, *Brit. M. J.* **2**:778 (Nov.) 1946.

10. Aycock, W. L., and Ingolls, T. H.: Maternal Disease As a Principle in the Epidemiology of Congenital Anomalies with a Review of Rubella, *Am. J. M. Sc.* **212**:366, 1946.

11. Wesselhoeft, C.: Rubella: German Measles (Concluded), *New England J. Med.* **236**:978 (July) 1947.

Thus it would appear that the incidence of cataract formation during the first three months is not as high as was originally believed. In this regard, it is interesting that there were no abnormalities of the lens in 2 of the specimens (2 and 4) for which there was a history of rubella during the first three months of pregnancy.

In discussing the low percentage of defects encountered in the American series, Swan, Tostevin and Black<sup>8</sup> suggested that there may be two strains of virus which produce rubella, one with, and one without, an affinity for embryonic tissues.

It is also of interest that in the preliminary report of Dr. Miller's committee, already mentioned, there was no evidence of cataract formation when rubella occurred after the third month of pregnancy. Thus, in specimen 3, the eye of an embryo from a woman who had rubella at the end of the third month, one would not expect to find cataract formation.

Bardram and Broendstrup,<sup>12</sup> in a review of this subject, stated that if fetal morbidity should prove to be fairly high, the question of therapeutic abortion must certainly be taken into consideration, especially since the effect of convalescent serum or similar therapy has not been ascertained. Swan and Tostevin<sup>4</sup> also stated the belief that, in the absence of effective prophylaxis, therapeutic abortion is entirely justifiable in the case of any woman who has rubella in the first four months of pregnancy. Other observers have voiced the same conviction.

This matter was discussed with Dr. Herbert Traut, professor of obstetrics and gynecology at the University of California. He stated that in the opinion of many leading obstetricians the termination of pregnancy in rubella is justifiable only under certain conditions: There must be a definite, unquestionable diagnosis of rubella in a severe epidemic. The infection must have occurred in the first trimester of pregnancy. From the ophthalmologic standpoint, clinical observations and the study of a limited number of embryos seem to corroborate these opinions.

Bardram and Broendstrup<sup>12</sup> suggested that all young girls be exposed to rubella as a prophylactic measure, since the mortality for all ages is reported to be only 1:50,000.

#### SUMMARY

The changes in the eyes of an 11 week old embryo are described. The mother had contracted rubella during the latter part of the second month of pregnancy. Both eyes of the embryo showed cataract formation.

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12. Bardram, M., and Broendstrup, P.: Maternal Rubella Pregnancy As a Cause of Congenital Cataract and Other Congenital Malformations, *Acta. ophth.* 25:352, 1947.

In addition, the findings in 3 other embryos are reported. The eyes showed no cataract formation.

A review of the literature and an examination of 5 specimens from mothers who had rubella during the first three months of pregnancy bear out the clinical findings that cataract formation is seen in a definite percentage of offspring in cases of maternal rubella. However, rubella contracted during the first trimester does not always result in changes in the lens.

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## CYCLODIALYSIS

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CYCLODIALYSIS as an operation for the relief of increased intraocular pressure has gained in favor with the staff of the ophthalmologic clinic at the University of Iowa until at present it is our operation of choice for chronic noncongestive wide angle or narrow angle glaucoma, hydrophthalmos and certain types of secondary glaucoma, notably that after cataract extraction. This paper is a report on the results of 100 consecutive operations made, with one exception, on patients with chronic primary glaucoma and followed for at least one year.

The literature on this operation has been covered thoroughly in the excellent reviews of Salus<sup>1</sup> in 1920 and Sugar<sup>2</sup> in 1947. Apparently, the first attempt to create an opening between the anterior chamber and the suprachoroidal space was reported by Quereghni<sup>3</sup> almost fifty years ago. However, Heine<sup>4</sup> (1905) devised the operation now known as cyclodialysis.

The purpose of each of the many operations for glaucoma is to lower and maintain within normal limits the damaging increased intraocular pressure. If one could only eliminate "maintain"! Cyclodialysis has been criticized severely by many surgeons because of its lack of permanent results. But what operation for glaucoma is invariably, or even usually, permanent? My personal opinion, substantiated by thirty years of experience, is that the tension after many so-called successful operations for glaucoma may, and often does, become elevated again after one, five or even ten or fifteen years. Only surgeons with little experi-

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From the Department of Ophthalmology, State University of Iowa College of Medicine.

1. Salus, R.: Die Zyklodialyse, *Klin. Monatsschr. f. Augenh.* **64**:433, 1920.

2. Sugar, H. S.: Cyclodialysis: A Follow-Up Study, *Am. J. Ophth.* **30**:843, 1947.

3. Quereghni, F.: Faits et raisons qui expliquent l'action de la sclero-iridectomie et des autres operations succedanees (sclerotomie et incision de l'angle iridocorneen) dans le traitement du glaucome, *Ann. d'ocul.* **123**:441, 1900.

4. Heine, L.: Die Cyklodialyse, eine neue Glaukomoperation, *Deutsches med. Wchnschr.* **31**:284, 1905; *Zur Therapie des Glaukoma*, *Ber. ü. d. Versamml. d. ophth. Gesellsch.* **32**:3, 1906.

ence or those who do not follow carefully their results are optimistic about the surgical treatment of glaucoma.

Heine's original theory regarding cyclodialysis has been proved; i. e., the operation creates an opening between the anterior chamber and the supracorneal space; the aqueous is drained into this space and absorbed. Elschvig<sup>5</sup> (1932) demonstrated microscopically that a permanent cleft was established where the ciliary body had been separated by operation from the scleral spur. Vannas<sup>6</sup> in 1935 first reported gonioscopic evidence of a cleft in the angle of the anterior chamber after a successful cyclodialysis, a finding confirmed by Barkan and associates,<sup>7</sup> Sugar,<sup>8</sup> Burr<sup>9</sup> and others (fig. 1).

Heine's original technic of cyclodialysis has been modified by a number of surgeons, some of whom combined it with iridectomy, sclerectomy or iridencleisis. Others implanted foreign substances, such as horsehair, silk thread, eggshell membrane or magnesium, in an attempt to keep the

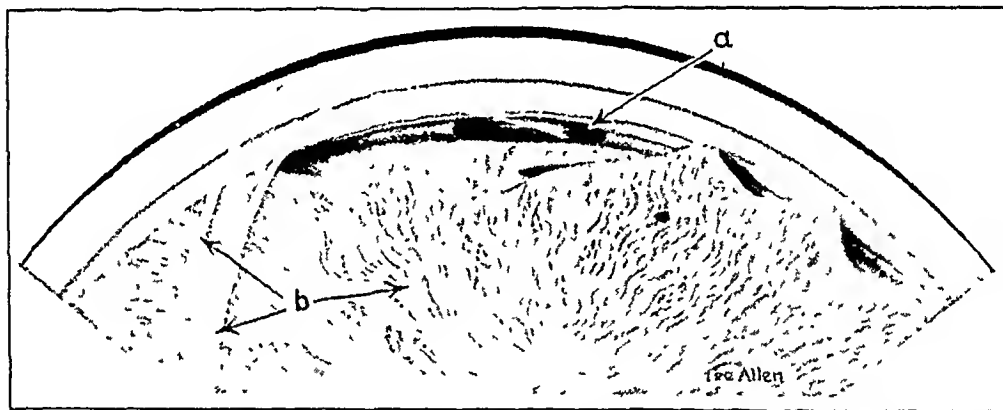


Fig. 1.—Angle of the anterior chamber as seen with the gonioscope and slit lamp: (a) cleft after a successful cyclodialysis; (b) optical section with the slit lamp beam.

cleft open. Blaskovics<sup>10</sup> modified the method of separating the ciliary body from the scleral spur and entitled it "inverse cyclodialysis"—the spatula was swept from the supracorneal space into the anterior chamber throughout the entire region of dialysis, and not from the anterior chamber toward the supracorneal space, as in the original operation.

5. Elschvig, A.: Zur Wirkungsweise der Cyclodialyse, Ber. ü. d. Versamml. d. deutsch. ophth. Gesellsch. **49**:277, 1932.

6. Vannas, M.: Zykoskopische Untersuchungen über das Verhalten des Strahlenkörpers nach der Heinischen Operation, Klin. Monatsbl. f. Augenh. **95**: 629, 1935.

7. Barkan, O.; Boyle, S. F., and Maisler, S.: On the Surgery of Glaucoma: Mode of Action of Cyclodialysis, Am. J. Ophth. **19**:21, 1936.

8. Sugar, H. S.: Gonioscopy and Glaucoma, Arch. Ophth. **25**:674 (April) 1941.

9. Burr, S. P.: Personal communication to the authors.

10. Blaskovics, L.: Cyclodialysis inversa, Szemészet **70**:5, 1935.



## CYCLODIALYSIS

*Indications for Operation.*—An operation for glaucoma is indicated when the intraocular pressure is elevated to such an extent that, in spite of drug therapy or any previous operation or operations, there is progressive loss of visual field. What is the average tension, as measured with the tonometer, above which one may expect trouble? It is our belief that a tension of over 22 mm. of mercury (Schjøtz) is usually pathologic. The field of vision should be checked carefully and repeatedly under identical conditions, i. e., the same size targets, at the same distance, with identical illumination and by the same technician.

It is suspected that in many cases in which the tension is found always to be within normal limits but the field is shrinking gradually there is at times an elevation of tension during the night.

Undoubtedly, early operation is best, i. e., before much loss of field occurs and before too many adhesions have formed in the chamber angle. But one must consider the age and life expectancy of the patient and the possible complications of operation, especially postoperative cataract. Indications for cyclodialysis vary with the surgeon; e. g., Ernst Fuchs resorted to it only after other operations had failed, while Barkan recommends it for both the wide angle and the narrow angle type of chronic noncongestive glaucoma and for certain types of secondary glaucoma. Although many surgeons apparently are not enthusiastic about this operation, it may be stated that some with great experience, namely, Elschmig, Blaskovics, Grosz and Gradle, employed the procedure often. Probably surgical results depend somewhat on the choice of cases and the technic of operation. Our personal feeling is that cyclodialysis is the operation of choice for any type of noncongestive glaucoma, for hydrophthalmos and for secondary glaucoma after cataract extraction, and as a second or third operation after any unsuccessful previous surgical attempt to lower the tension in cases of the aforementioned types of glaucoma. Furthermore, in many cases chronic congestive glaucoma responds to cyclodialysis. At the Iowa clinic the operation has grown gradually in favor until at present it is performed in more than 75 per cent of the cases of glaucoma in which surgical treatment is necessary.

*Advantages of Cyclodialysis.*—That the operation is comparatively harmless even in the hands of rather inexperienced surgeons is conceded. Certainly, it is less dangerous than any of the external filtering operations. Only in rare instances are harmful effects encountered, even though the cleft closes. The operation does not mar the appearance of the eye; it may be repeated once or several times, and secondary infection is exceedingly rare. The chances of success are lessened somewhat if the operation is repeated in the area of a former dialysis.

*Disadvantages.*—As occasionally occurs in any operation for glaucoma, the tension may not be lowered at all, or, if it is lowered, it may rise again sooner or later. Gát<sup>11</sup> stated that one disadvantage is the delay of three or four days between the operation and effective lowering of the intraocular pressure—we have not found it so with our present technic. Gát recommended posterior sclerotomy to lower the tension for the first few days, but it is believed that this procedure is not only unnecessary but inadvisable. Rarely profuse bleeding may occur at the time of operation or during convalescence. Cyclodialysis has been criticized for its lack of permanent results, but in our hands its effects have been as permanent as those of other operations.

*Gonioscopic Studies.*—It is imperative that the entire angle be examined carefully with the gonioscope and slit lamp in an effort to determine the proper site for operation. If possible, the dialysis is made in an area in which the angle is open and in which no large blood vessels are seen.

After operation a cleft in the chamber angle may be observed in almost every patient with a normal or low intraocular pressure. Occasionally the iris hump obscures the angle, but instillation of a miotic may allow study of this region.

*Preoperative Routine.*—Miosis is maintained up to the time of operation, and it is well to instil a strong miotic, such as 0.5 per cent solution of physostigmine salicylate, in each eye an hour or two before the patient is taken to the operating room. Typhoid H antigen, in a dose of 15,000,000 killed bacilli injected intravenously, is administered routinely on the day before operation. If the tension is high, 100 cc. of 50 per cent sorbitol may be injected into the vein the evening prior to operation, as advocated by Sanford Gifford. As a sedative, sodium bromide, grains 30 (2 Gm.), and chloral hydrate, grains 15 (1 Gm.), are administered in milk by mouth the night before operation and the administration is repeated the following morning one hour before the patient goes to operation. Pentobarbital sodium, grains 1½ (0.1 Gm.), may be added if necessary.

Local anesthesia is entirely satisfactory. A 0.5 per cent solution of tetracaine hydrochloride is instilled into the conjunctival sac every two minutes for five instillations and a retrobulbar injection of 2 cc. of 2 per cent procaine hydrochloride solution with epinephrine hydrochloride (1:20,000) is made into the muscle cone immediately behind the globe; this not only results in deep anesthesia but also lowers the intraocular pressure. Akinesia is of assistance and is used routinely.

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11. Gát, L.: Ueber die Wirksamkeit der modifizierten Cyklodialyse, *Ophthalmologica* 114:106, 1947.

*Technic of Cyclodialysis.*—Several modifications of the original technic for cyclodialysis have been devised, the best known being Blaskovics' inverse cyclodialysis, described in 1935.

Barkan<sup>12</sup> advocated the use of a large conjunctival flap, a scleral incision 8 mm. back of the limbus and the injection of air for hemostasis and to make possible an immediate second dialysis in another quadrant.

The technic used at the Iowa clinic differs somewhat from both the original operation of Heine and Blaskovics' inverse cyclodialysis. As a rule, the superior temporal quadrant is chosen as the site of operation, since it is believed that the cleft is more liable to remain open permanently for the reason that if any hemorrhage occurs, the blood tends

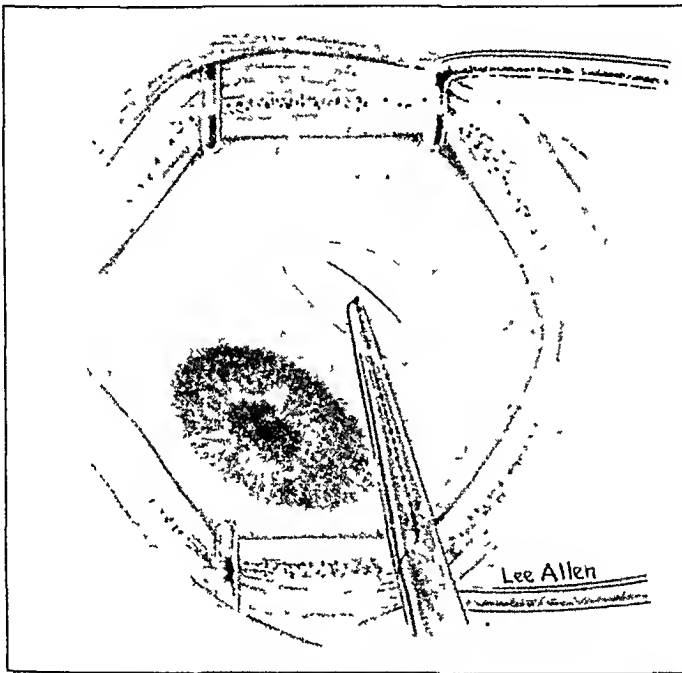


Fig. 2.—Scleral fixation with a 0000 silk suture grasped with a small hemostat.

to gravitate toward the lower portion of the anterior chamber and in this manner is carried away from the cleft. Furthermore, the dialyzed ciliary body has a tendency to sag downward and keep the cleft open if the patient is kept in a sitting position.

The conjunctival incision is approximately 8 mm. in length and is made parallel to and from 6 to 8 mm. back of the limbus, thus exposing an area of sclera in the upper (or lower) temporal quadrant. Next, the area for the intended scleral incision is selected between the insertions of the tendons of the lateral and superior rectus muscles.

12. Barkan, O.: Cyclodialysis, Multiple or Single, with Air Injection: An Operative Technique for Chronic Glaucoma, *California Med.* 67:78, 1947.

Before the incision is made, a scleral fixation suture of 0000 silk is placed just anterior to the area of intended incision (fig. 2); the silk is grasped near the sclera with a mosquito hemostat, and the loose ends are cut away. Or one may tie two knots near the sclera, cut off the loose ends of silk and grasp the knots with forceps. Fixation by either method is quite secure. In order that undue bleeding in the area of the

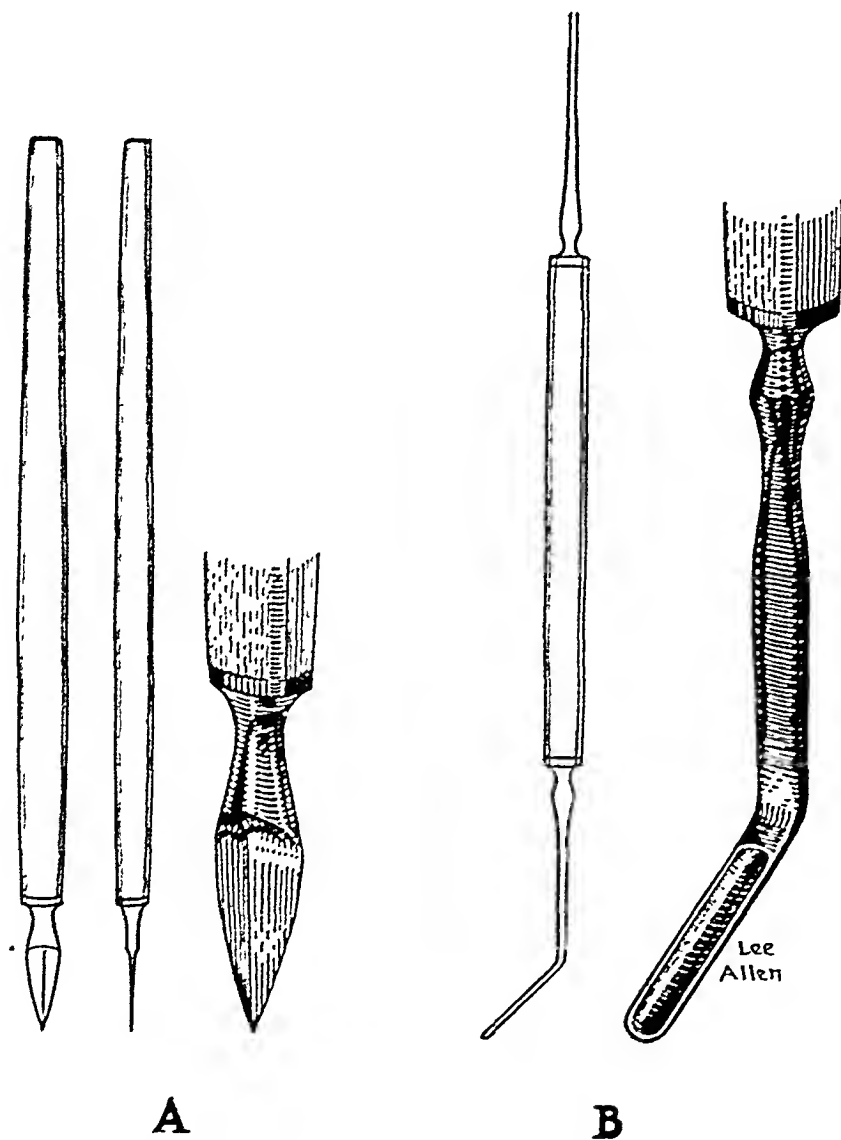


Fig. 3.—*A*, sclerotome; *B*, grooved spatula.

incision may be eliminated, a small muscle hook is heated slightly over an open flame and the sclera over the area of incision is touched very lightly with the heated instrument, thus coagulating the vessels. Next, the incision itself is made with either a sclerotome (fig. 3) or a Graefe knife; this incision is made approximately 4 mm. back of the limbus and is 3.5 to 4 mm. long, concentric with the limbus and slanted slightly forward as it passes through the sclera. Approximately one-half the

thickness of the sclera is incised with the first sweep of the knife; then, with the sharp point of the knife, the scleral tissue is picked carefully from within outward, great care being taken to cut all the fibers but

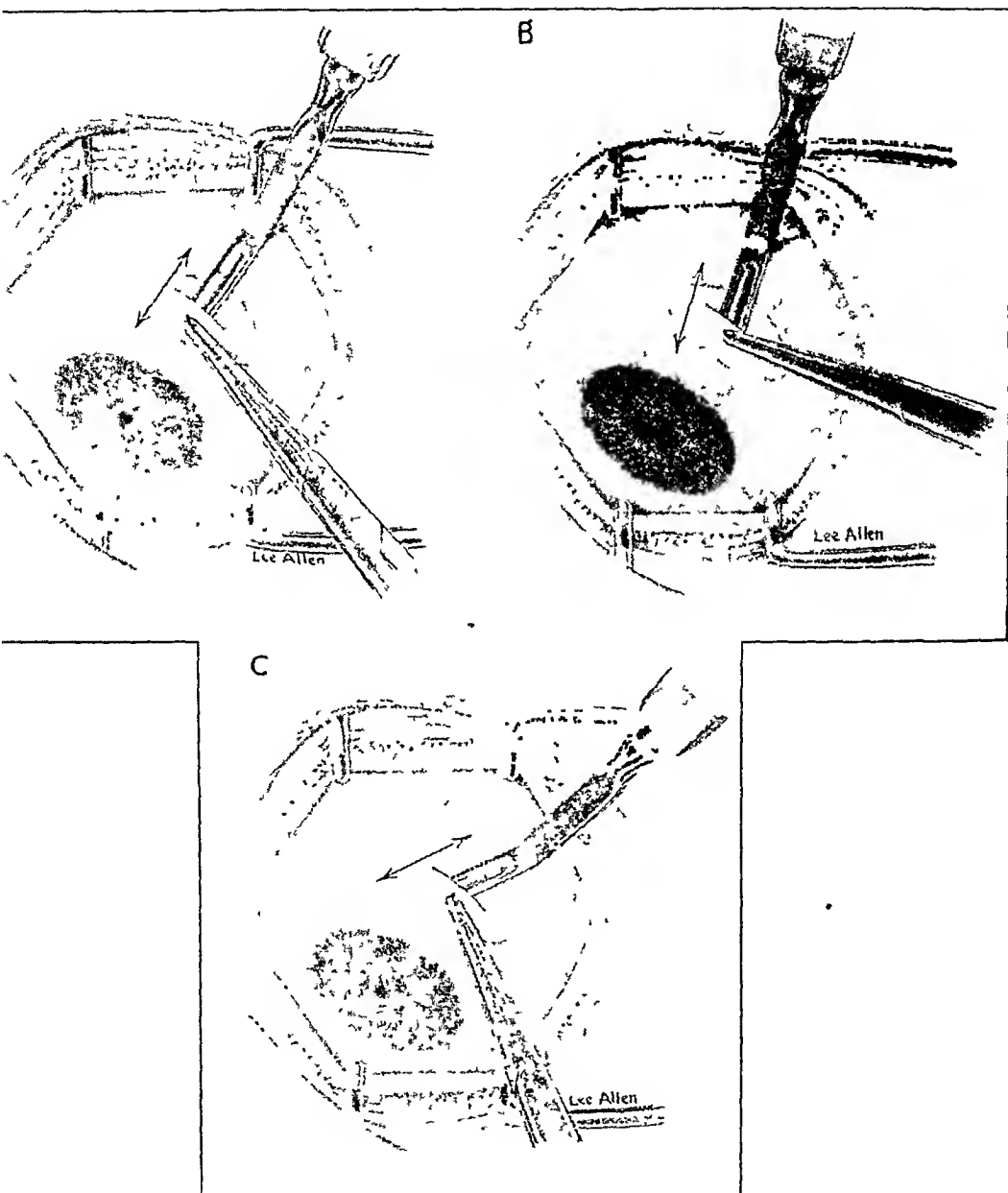


Fig. 4.—*A*, spatula passed inward and withdrawn in the direction of arrows, *B*, later stages of dialysis. Arrows indicate direction of the spatula. *C*, still later stages of dialysis.

to avoid injuring the underlying uvea. One must not pull on the fixation suture; otherwise the incision may tend to extend forward within the sclera rather than pass through, as intended.

A special grooved spatula (fig. 3), first recommended by Laird,<sup>13</sup> is used for the actual dialysis. The anterior lip of the scleral wound is lifted with the fixation suture, and the spatula is made to depress the posterior lip; then, with the tip pointing forward, the instrument is inserted slowly and carefully, its tip hugging the inside of the sclera at all times. The spatula is not at any time pointed toward the vitreous. As soon as the tip of the instrument is viewed in the periphery of the anterior chamber (fig. 4 *A*), the spatula is withdrawn slightly, and then, by repeated thrusts of the tip of the instrument through the region of the scleral spur (fig. 4 *B* and *C*), almost one-half the attachment of the

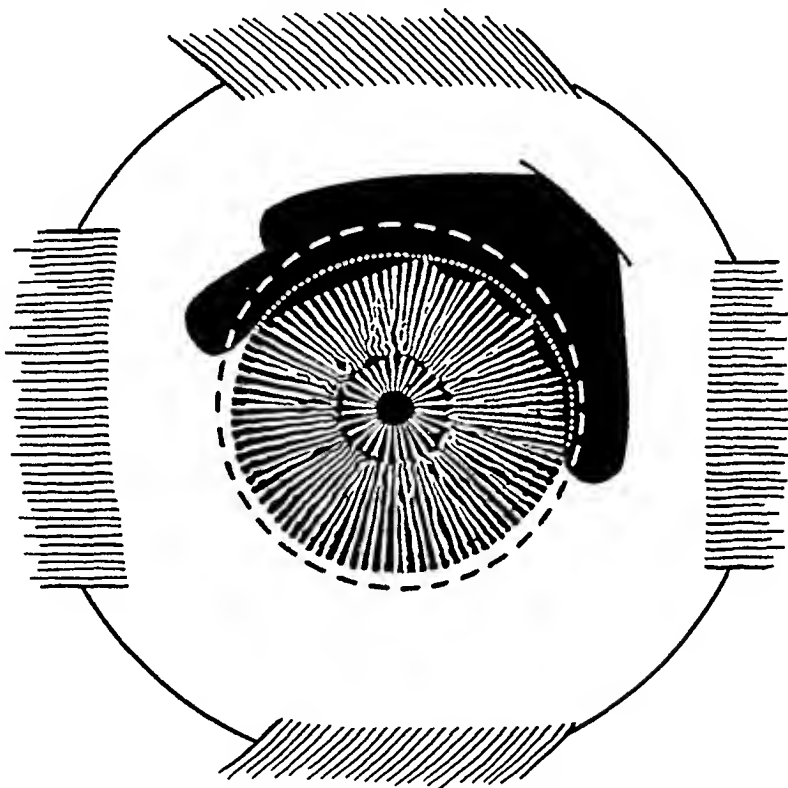


Fig. 5.—Extent of dialysis as shown by darkened area.

ciliary body is torn loose (fig. 5). The sweeping motion as advocated by Heine, or that made in the opposite direction, as described by Blaskovics, is not used. Great care is exerted not to enter far into the anterior chamber, since it is believed that the endothelium of the cornea, Descemet's membrane and the crystalline lens are then more liable to severe injury.

The groove in the spatula is utilized to draw the blood from the area of operation during the few minutes in which bleeding usually occurs. The blood is withdrawn by applying sharp-pointed, moistened, sterile cotton dental swabs to the portion of the groove situated just

13. Laird, R. G.: Personal communication to the authors.

outside the incision. In this way, little or no blood remains in the region of the cleft or the angle of the anterior chamber after the operation has been completed. It is believed that this technic is preferable to injection of air. It certainly keeps the cleft free from any hemorrhage which may organize at some later time and close the communication between the anterior chamber and the supraciliary space. Of course, it does not prevent the occasional delayed hemorrhage which may occur during convalescence.

As for actual dialysis, it is believed that the result is oftener permanent when almost one-half the attachment of the ciliary body is separated from the scleral spur. We feel that a smaller dialysis is much more likely to close and that this may be the reason that many surgeons object to this operation on the basis of lack of permanent results.

Injury to the anterior ciliary arteries may cause excessive hemorrhage. Consequently, during the process of dialysis the spatula is kept in front of these vessels. The anterior ciliary arteries perforate the sclera approximately 2 mm. anterior to the insertion of the tendons of each of the rectus muscles. The long posterior ciliary arteries are not injured, since they usually enter the posterior portion of the ciliary body and therefore are too far back unless the incision is made 7 to 8 mm. behind the limbus. With the technic here described, it is certainly unusual to injure these vessels.

In 1943 Randolph<sup>14</sup> first reported injection of air following cyclo-dialysis. Barkan expressed the belief that his technic of single or multiple cyclo-dialysis with injection of air produces less trauma and gives more permanent results than other methods.

The scleral wound may or may not be closed with a suture; a short incision, such as that used in our technic, usually does not require closure. The conjunctiva is closed with 0000 surgical gut or with 000000 silk sutures.

*Postoperative Routine.*—Immediately after operation 0.25 per cent solution of physostigmine salicylate is instilled in an effort to keep the dialyzed portion of the ciliary body away from its attachment. A dressing is applied over the closed lids and left in place for six to eight hours. The patient is asked to lie in bed twenty-four hours with the head elevated approximately 45 degrees and is requested to remain quiet as a guard against bleeding. Pilocarpine nitrate, 1 per cent solution, is instilled twice a day. If undue redness develops or evidence of early iritis appears, 5 per cent solution of cocaine hydrochloride and 1 per cent epinephrine bitartrate jelly are instilled once a day—this medication dilates the pupil temporarily and prevents formation of synechias. After this treatment the pupil is again contracted with pilocarpine. The patient

14. Randolph, M. E.: A New Cyclo-dialysis Instrument, *Am. J. Ophth.* **26**:187, 1943.

is allowed out of bed after the first day. Gentle massage, an important part of the postoperative treatment, is instituted on the day following operation and is continued twice daily for several weeks, being carried out by the physician while the patient remains in the hospital and after this time by the patient himself. During the first few postoperative days the massage must be gentle; otherwise it may cause hemorrhage.

*Complications.*—Complications may be encountered at the time of operation or during convalescence. Of the complicating factors which occur at operation, the one reported to be commonest is hemorrhage. With our present technic, this occurs rarely, perhaps because by preliminary gonioscopic examination we have learned the location of any large vessels in the angle of the anterior chamber and, furthermore, because we have exerted care to stay in front of the area in which the anterior ciliary arteries extended from the sclera into the ciliary body. With this technic of detaching the ciliary body from the scleral spur, it is unnecessary to sweep the spatula over the region of the anterior ciliary vessels. Furthermore, by removing the blood which flows outward along the grooved spatula and by continuing to do this until bleeding stops, it is unusual for an eye to contain much free blood when the patient leaves the operating room.

Delayed hemorrhage is another matter. Bed rest for twenty-four hours, with limited activity for a few days, is apparently the best preventive. Of the 100 cases reported here, there were 3 with severe postoperative hemorrhage occurring on the first or second day after operation. One of these eyes had an eventual rise in tension; a second became blind, but not painful, and the third had to be enucleated. The belief that large, and perhaps some moderate-sized, hemorrhages are prone to result in closure of the cleft is probably true.

Occasionally, especially with inexperienced surgeons, all the scleral fibers may not be severed at the time of incision, and undue pressure with the spatula may result in sudden plunging of this instrument through the choroid and into the vitreous. Such a complication may be prevented if all the scleral fibers are cut, if only gentle pressure is used to insert the spatula into the wound and if the anterior lip of the wound is lifted with the fixation suture and the direction of the spatula is forward and along the inside of the sclera, rather than toward the choroid and vitreous. This complication occurred in 2 of our cases; the tension was not controlled. Even though vitreous does present in the wound, the operation may be completed as usual.

If the spatula is not kept against the inside of the sclera, it may penetrate the root of the iris, and the tip will then pass into the posterior chamber. Injury to the lens may follow.

At times, when dense anterior peripheral synechias are present, the spatula meets with strong resistance. It is well to proceed carefully and to maintain control over the instrument at all times.



Lacerations of Descemet's membrane result from pressure with the spatula against the posterior surface of the cornea. Therefore, one must use great care to insert the spatula only a short distance into the anterior chamber, and it must be kept between and away from the posterior surface of the cornea and the root of the iris. If there is severe injury to the cornea, permanent opacity may result.

The commonest late complication, if it may be called a complication, is closure of the cleft with recurrence of the increased intraocular pressure. The operation is designated as a surgical failure if this occurs within a period of a few weeks or months. The tension was not controlled in 21 of the 100 cases under discussion. Occasionally the cleft may not close for several years, or the closure may follow other operative intervention, e. g., cataract extraction.

Changes in the refractive error are common after cyclodialysis; however, they often disappear gradually. Usually the refractive error is increased; i. e., hypermetropia is lessened or myopia increased.

Cataract is a common late complication. Of course, if the operation is made improperly and the lens is injured by the spatula, a cataract may develop with great rapidity. However, this complication is rare, but the slow development of cataract after a period of from one to ten years is common. It is our belief that after cyclodialysis, as well as after any of the external filtering operations, cataract not infrequently develops. After long experience, one of us (C. S. O'B.) has concluded that opacities in the lens develop gradually after operation for glaucoma in many more patients than the literature would lead one to believe. Therefore, in the decision to operate or not to operate for glaucoma, this factor must be considered, and I should go so far as to state that a patient should be warned of the possibilities of gradual loss of central vision and of eventual cataract extractions. Of the 79 cases of successful operation in this series of 100, there were some loss of central visual acuity in 23 eyes, loss of one line (Snellen chart) in 15 eyes, loss of two lines in 2 eyes and loss of more than two lines in 6 eyes. Our records did not state always the cause of visual loss, but often it was due to cataract.

Cataract extraction is more easily made after cyclodialysis than after external filtering operations, such as Elliot's trephine operation or the Lagrange procedure. One should suture the cataract wound securely in order that the anterior chamber will reform rapidly and in this manner lessen the chance of closure of the cyclodialysis cleft.

Another infrequent complication is low grade iridocyclitis, which may appear during the first or second week after operation. As a rule, this is a mild inflammation and may be controlled with a daily intravenous injection of typhoid H antigen. In order to prevent posterior synechias, one dilates the pupil temporarily, daily or every other day, with a 5 per cent solution of cocaine hydrochloride, followed with instillation

of 1 per cent epinephrine bitartrate jelly—this results in the pulling away of any newly formed adhesions. The administration of a 1 per cent solution of pilocarpine nitrate morning and evening is continued as usual. We were faced with this complication in 6 eyes, but in only 2 of them was the tension uncontrolled.

Hypotony is a rare complication of cyclodialysis—as a matter of fact, much rarer than after the external filtering operations. Even with large dialysis, such as is made in the Iowa clinic, tensions of 12 to 14 mm. extending over any prolonged period are extremely rare. It occurred in only 1 of the 100 cases.

In 1 eye there was some hemorrhage into the vitreous. Prolapse of a small knuckle of ciliary body has been seen, but this complication did not occur in this series of cases. Subluxation of the lens has been reported, but this we have not encountered, and it must be very unusual. Retinal detachment is also reported as a complication. A cystoid or ectatic scleral scar has been mentioned in the literature.

*Results of Operation.*—Cyclodialysis differs little from many other operations on the eye in that the results of the operation depend somewhat on the patient and the individual response of the eye to surgical intervention; they depend greatly on the surgeon's choice of operation, technical skill and surgical judgment.

Successful results from this operation have been reported in as few as 20 per cent of cases (Troncoso<sup>15</sup>) and in as many as 90 per cent (Barkan<sup>12</sup>).

What constitutes a successful result? The eye should be white and free from inflammation; the tension should remain within normal limits, and there should be no further loss of visual field. The last is the real criterion. Oftentimes there will be a slow but progressive loss of central vision as the result of changes in the lens, even though the aforementioned criteria for a successful result have been fulfilled. The question arises: Is this a successful result? Certainly, the patient has been freed from increased pressure and permanent loss of vision. Consequently, while it has not done all that may be desired, the operation must be considered successful, since if the tension is controlled it has accomplished its purpose. According to these criteria, the results in 79 of the 100 cases reported here were successful; i. e., the eye was not inflamed, the tension was 22 mm. of mercury or less (Schiotz) and there was no loss of field for at least one year. In 24 of these 79 cases one or more previous operations had been performed for glaucoma.

The operation may be immediately successful but be followed within a few days, weeks or months by the return of increased intraocular

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15. Troncoso, M. U.: Cyclodialysis with Insertion of a Metal Implant in the Treatment of Glaucoma, *Arch. Ophth.* 23:270 (Feb.) 1940.

pressure, or it may be permanently successful. Perhaps the word "permanent" should not be used here, since a certain percentage of so-called permanent results eventually prove to be otherwise. We do not consider the operation effective unless the tension remains within normal limits (22 mm. of mercury or less, [Schiotz]) with or without the use of miotics for at least one year. Certainly, one should never release from observation a patient who has once had glaucoma, no matter how successful the operation may seem.

In eyes in which the tension has been reduced, examination with the gonioscope almost always reveals an open cleft in the angle of the anterior chamber.

In most cases of successful operation the tension is from 14 to 18 mm. (Schiotz) for a few weeks or months and then it gradually climbs to 20 to 22 mm. Some patients require massage or miotics, or even both, to control the pressure. Perhaps in patients who have an increased pressure which responds to miotics the iris plugs the cleft unless the pupil is contracted and the iris is pulled out of the angle.

Every ophthalmologist encounters patients in whom the postoperative intraocular pressure apparently remains within normal limits but the visual field continues to contract. Is this the type of patient whose eye cannot withstand an average normal intraocular pressure and whose tension must be less than the average to preserve function? Or is the condition a cavernous atrophy of the optic nerve? Or what is it? We believe that many patients of this type must have an elevated intraocular pressure at times, probably during the night; of course, this is not true of all such patients, and sometimes the loss of field remains inexplicable.

In behalf of cyclodialysis, it may be stated that the operation may be repeated one or more times with an excellent chance of success if the second operation is made in another area, but with some chance even if the operation is repeated in the area of previous dialysis. Some surgeons believe that second operations are almost always ineffective, but this is open to question; e. g., in 2 eyes the third cyclodialysis controlled the tension.

#### SUMMARY AND CONCLUSIONS

Cyclodialysis is the operation of choice for chronic noncongestive glaucoma (wide angle and narrow angle types); in an opinion based on data other than those discussed in this paper, it is the operation of choice for hydrophthalmos and for the secondary glaucoma which follows cataract extraction.

The operation is oftener successful if extensive dialysis is performed, i. e., separation of almost one-half the attachment to the scleral spur. Bleeding must be controlled if results are to be satisfactory.

The operations reported here were performed by various members of the staff (including the resident staff), and almost all were performed prior to 1946. It is believed that the results are better at present, since improvements in technic have been made.

The results of 100 consecutive operations on eyes with chronic primary glaucoma are summarized in the accompanying tabulation.

	No. of Cases
Cyclodialysis .....	100
Successful (for at least 1 year) .....	79
Unsuccessful .....	21
Reoperation (one or more times) .....	14
Cyclodialysis .....	5
Successful .....	1
Unsuccessful .....	4
Other operations .....	9
Complications	
Hemorrhage in anterior chamber .....	47
Severe .....	3
Moderate .....	7
Mild .....	37
Iridocyclitis .....	6
Severe .....	2
Mild .....	4
Loss of vitreous .....	2
Hemorrhage in vitreous .....	1
Hypotony .....	1
Diminution of visual acuity (usually cataract) .....	23

## DETACHMENT OF THE RETINA IN EARLY SARCOMA (MALIGNANT MELANOMA) OF THE CHOROID

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IN THE beginning of its growth sarcoma of the choroid does not cause detachment of the retina. It is after the tumor becomes larger that it causes the retina to separate from the choroid, and into the space thus formed an albuminous fluid is extravasated (serous detachment). Not infrequently the retina remains adherent to the head of the sarcoma—solid detachment—while along its sides the fluid presses the retina away from both the tumor and the choroid. The present paper is concerned only with the early stage of the detachment, before it has become total and before glaucoma has set in.

At a meeting of the Ophthalmological Society of Vienna in 1935, Salzmann<sup>1</sup> showed microscopic preparations of early sarcoma of the choroid in which, in addition to the ophthalmoscopically visible detachment of the retina confined to the neighborhood of the tumor, there existed on the opposite side of the fundus a circumscribed slitlike separation.

A short time afterward, A. Fuchs<sup>2</sup> reported 4 cases of a vesicular detachment of the retina immediately below the ora serrata. This detachment was far removed from the tumor and was apparently independent of the slitlike separation described by Salzmann, which was also present in all 4 cases. To the slitlike detachment, Fuchs gave the name *minimale Netzhautabhebung* (minimal retinal detachment) and to the one at the ora serrata, the name *Netzhautabhebung an der Ora serrata*. Thus, two new terms were added to the many in the nomenclature of retinal detachment.

In a second paper, Fuchs<sup>3</sup> reported 5 more cases of detachment at the ora serrata. As so often happens when one believes one has run

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1. Salzmann, M.: Klin. Monatsbl. f. Augenh. 1935, vol. 95; Ueber Früstadien des Sarkoms der Aderhaut und die histologischen Grundlagen des Augenspiegelbildes, Ztschr. f. Augenh. 88:185 (Feb.) 1936.

2. Fuchs, A.: Ueber umschriebene Netzhautabhebung an der Ora serrata bei beginnendem Sarkom der Aderhaut, Klin. Monatsbl. f. Augenh. 95:1 (July) 1935.

3. Fuchs, A.: Zur klinischen Bedeutung der umschriebenen Netzhautabhebung an der Ora serrata bei beginnendem Aderhautsarkom, Klin. Monatsbl. f. Augenh. 98:606 (May) 1937.

across something new in ocular pathology, Fuchs found, on consulting the literature, that his father, E. Fuchs,<sup>4</sup> had long before called attention to detachment at the ora serrata in a report of 2 cases.

#### PRESENT MATERIAL

To the reported 11 cases of circumscribed detachments of the retina, both minimal and at the ora serrata, associated with early sarcoma of the choroid, I am able to add 19 which were selected from the collection of sarcomatous globes in the museum of the Eno Laboratory at the New York Eye and Ear Infirmary. The tumors were of various shapes and sizes and were located in the posterior or the lateral portion of the fundus.

*Minimal Detachment.*—In 12 of the 19 cases, minimal detachment occurred at a distance from the primary detachment that surrounded the tumor. The height of the separation ranged from 0.125 to 0.2 mm.; only once did it attain 0.5 to 1 mm. The area of the fundus involved varied a great deal. In 5 cases it covered the entire side opposite the tumor, reaching as far as the ora serrata. At times the greater part of the retina appeared to be more or less detached (figs. 1 *A*; 2 *A*; 3 *A*; 4 *A* and *B*). Occasionally the detached area was very limited, being confined to the other side of the papilla (fig. 1 *B*).

In a number of cases there were several separate minimal detachments (figs. 2 *B* and *C*; 3 *B* and *C*). Some of these spaces may have been cross sections of irregular borders of one extensive and continuous detachment. As a rule, when the slits were multiple, one was found on the opposite side of the papilla and the other in the corresponding equatorial region.

*Oral Detachment.*—In 10 of the 19 cases there was a circumscribed vesicular detachment immediately behind the ora serrata or 1 to 2 mm. from it (figs. 1 *B*, *C* and *D*; 2 *B*, *C* and *D*; 3 *B* and *C*; 4 *C* and *D*). The height varied from 0.1 to 0.2 mm., several times attaining 1 to 2 mm. The extent of the detachment ranged from 1 to 4 mm., the greatest being 6 mm. In 4 cases there was a detachment at the ora serrata without a minimal detachment (figs. 1 *D*, 2 *D*, 3 *D* and 4 *C*). Of the cases of combined detachment, a small detachment occurred at the papilla in 1, and two slits, one next to the papilla and the other at the equator, in another.

*Proofs of Intravital Detachment.*—The fluid in the spaces had taken a deep pink color from its albuminous content, as is usual in cases of

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4. Fuchs, E.: Ueber Pigmentierung, Melanom and Sarkom der Aderhaut, Arch. f. Ophth. 94:43, 1917; Klin. Monatsbl. f. Augenh. 98:5, 1937.

sarcoma of the choroid, in contrast to the faintly stained Blessig's cysts at the ora serrata. Between the 2 fluid systems there was never any evidence of communication. Not infrequently cellular elements were seen in the subretinal fluid. The damage to the rods and

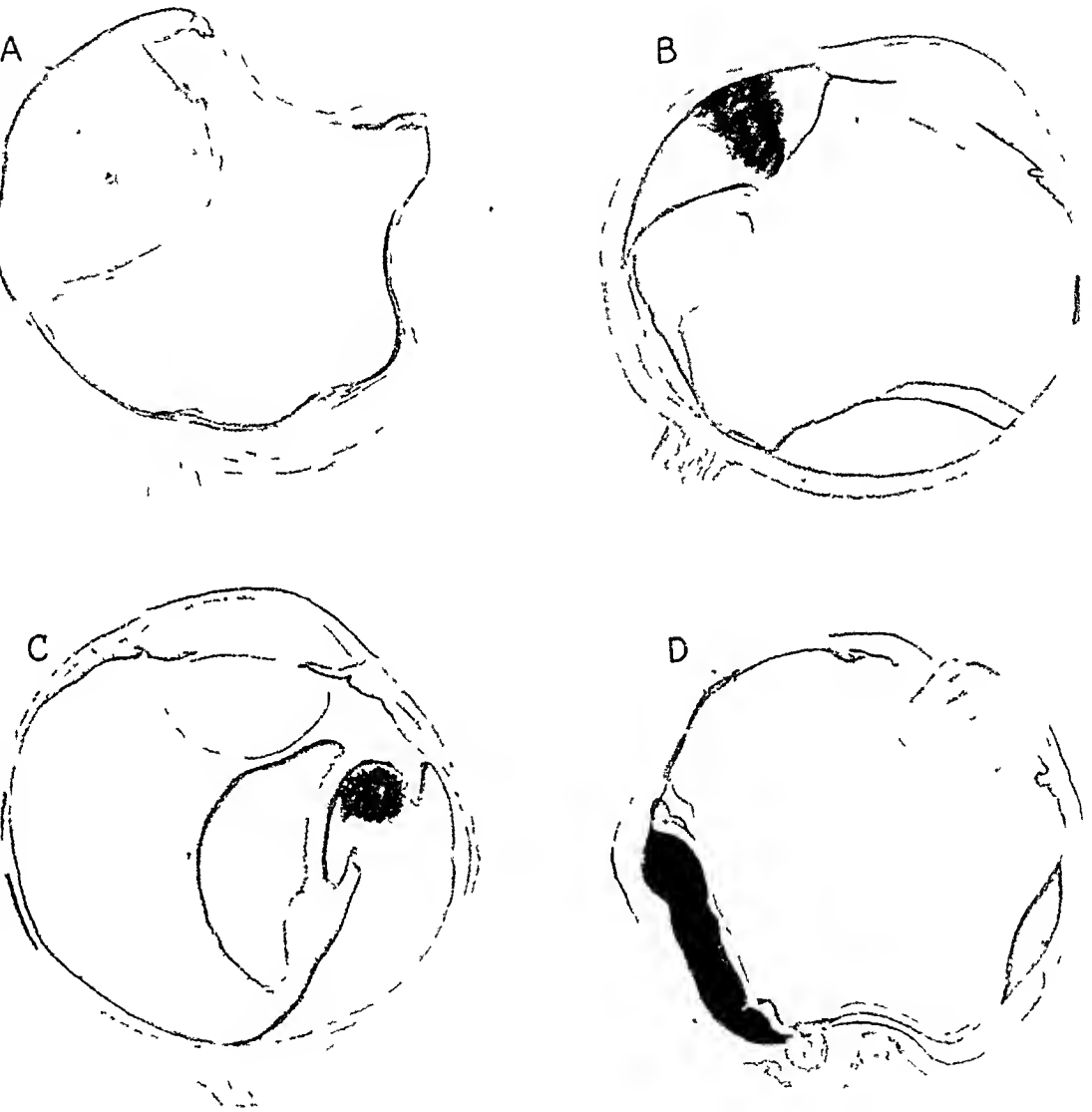


Fig. 1.—*A*, malignant melanosarcoma of the choroid and ciliary body. A minimal detachment embraces the entire opposite side. *B*, malignant melanoma of the choroid and ciliary body; circumpapillary minimal detachment opposite the tumor, with distant detachment at the ora serrata. *C*, melanosarcoma of the choroid, with two independent slitlike detachments opposite the tumor. *D*, vesicle-like detachment at the equator opposite the tumor. A long posterior artery is shown. A section of the cornea has been removed for keratoplasty.

cones was far greater than would probably have occurred, in the same period of time, in such small cavities in a case of spontaneous or

traumatic detachment. At many points the rods and cones were missing, and at others they had dissolved into drops, all of which indicated extraordinary toxicity on the part of the fluid.

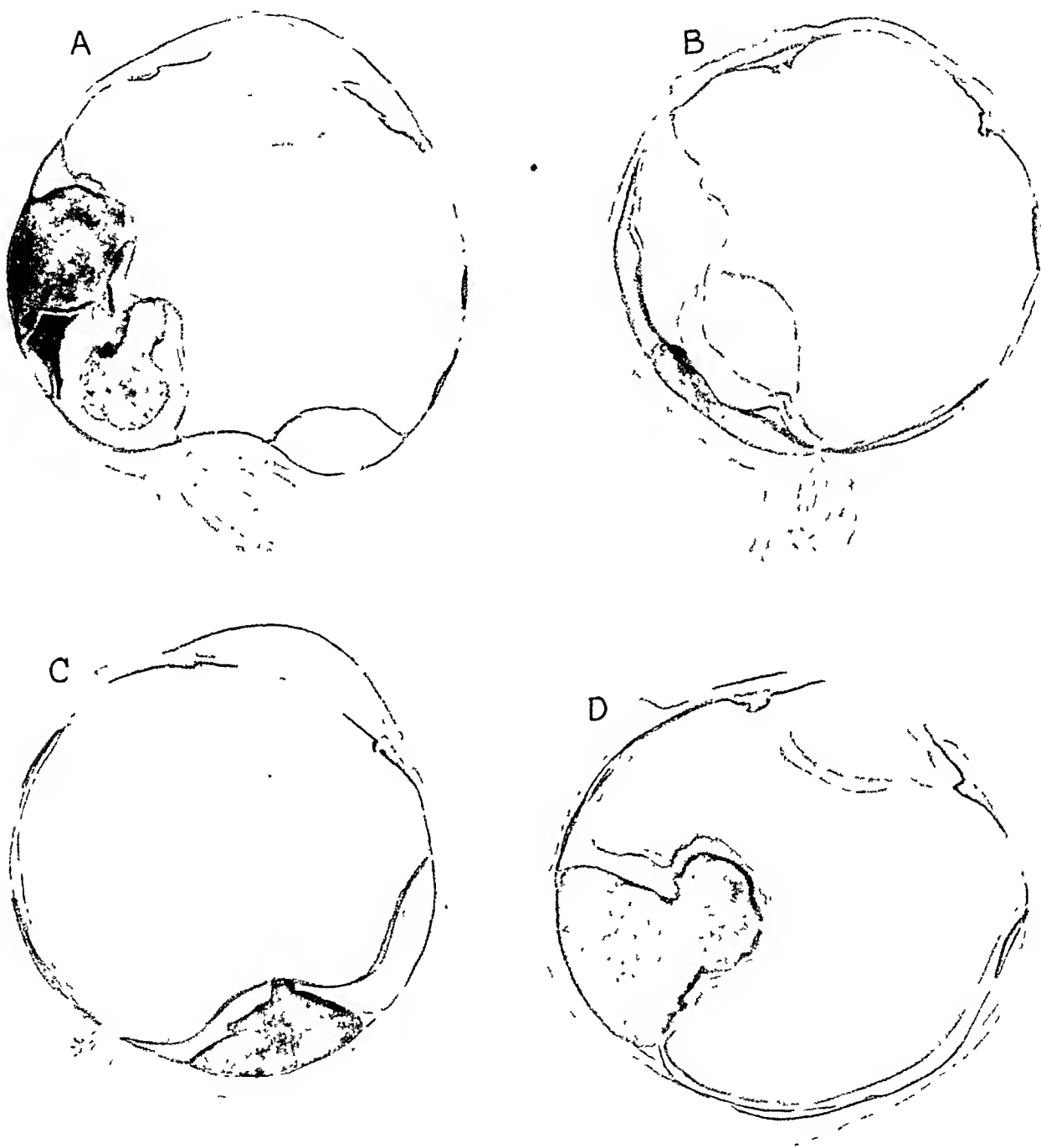


Fig. 2.—*A*, circumpapillary detachment; two separate minimal detachments opposite the malignant melanoma. *B*, independent, flat detachment at the ora serrata opposite the tumor, independent of the circumpapillary detachment. *C*, complete detachment on the side of the tumor and around the nerve head; independent, slitlike detachment at the ora serrata opposite the tumor. *D*, small slitlike detachment at the ora serrata opposite the tumor. A corneal section has been removed for keratoplasty.



RELATION OF MINIMAL RETINAL DETACHMENT AND DETACHMENTS AT THE ORA SERRATA

The slides available for study were cut in a meridional direction. In a given case of combined minimal detachment of the retina and

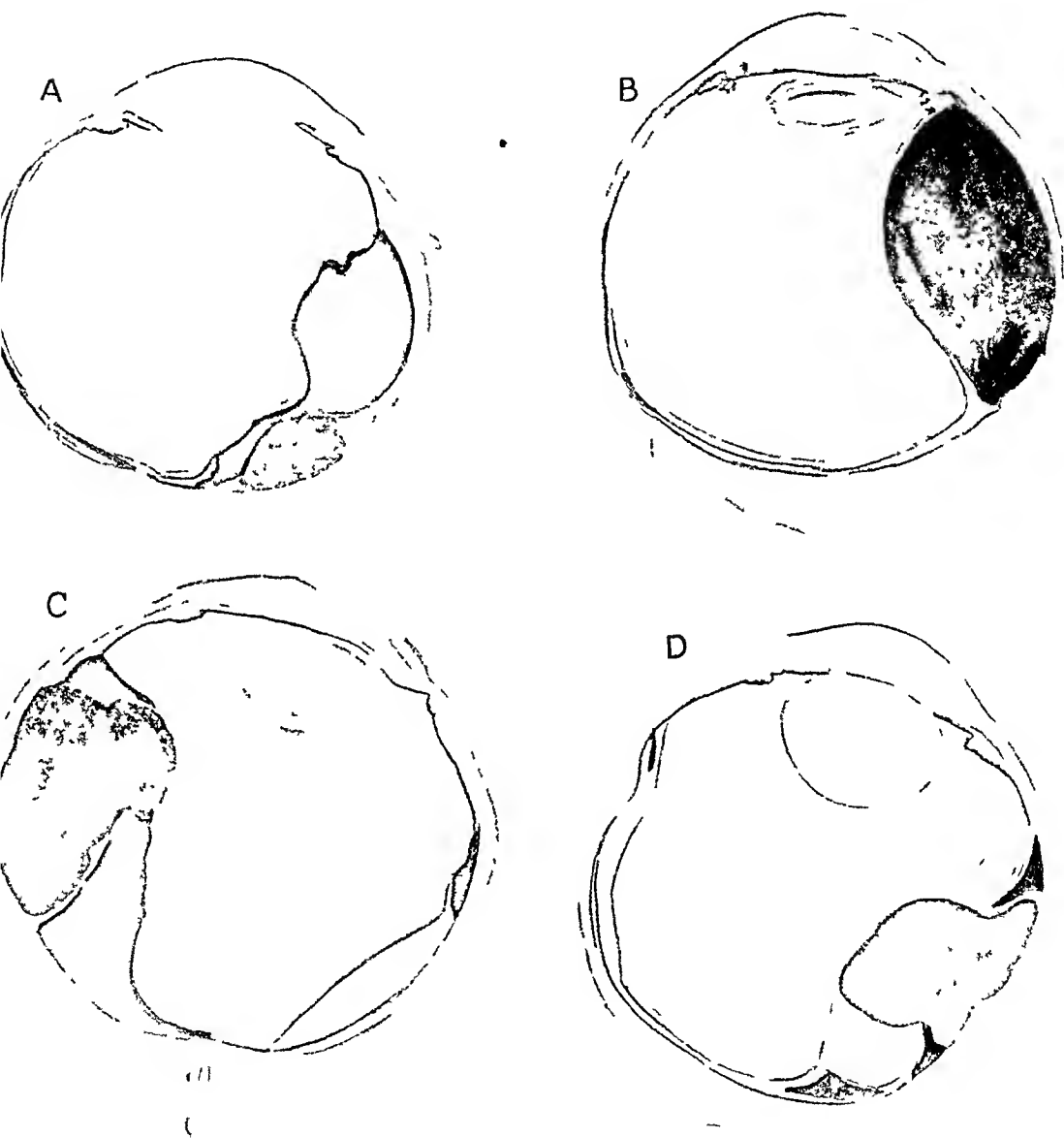


Fig. 3.—*A*, minimal detachment occupying the entire side opposite the tumor. *B*, three small minimal detachments opposite a large malignant melanoma. The retina has remained attached to the tumor. *C*, vesicle-like detachment at the ora serrata opposite the tumor. *D*, mere slitlike detachment opposite the mushroom-shaped malignant melanoma.

detachment at the ora serrata, frontal and serial sections might have proved the existence of a single continuous, thin sheet of serous fluid that had spread out from the primary fluid at the site of the tumor.

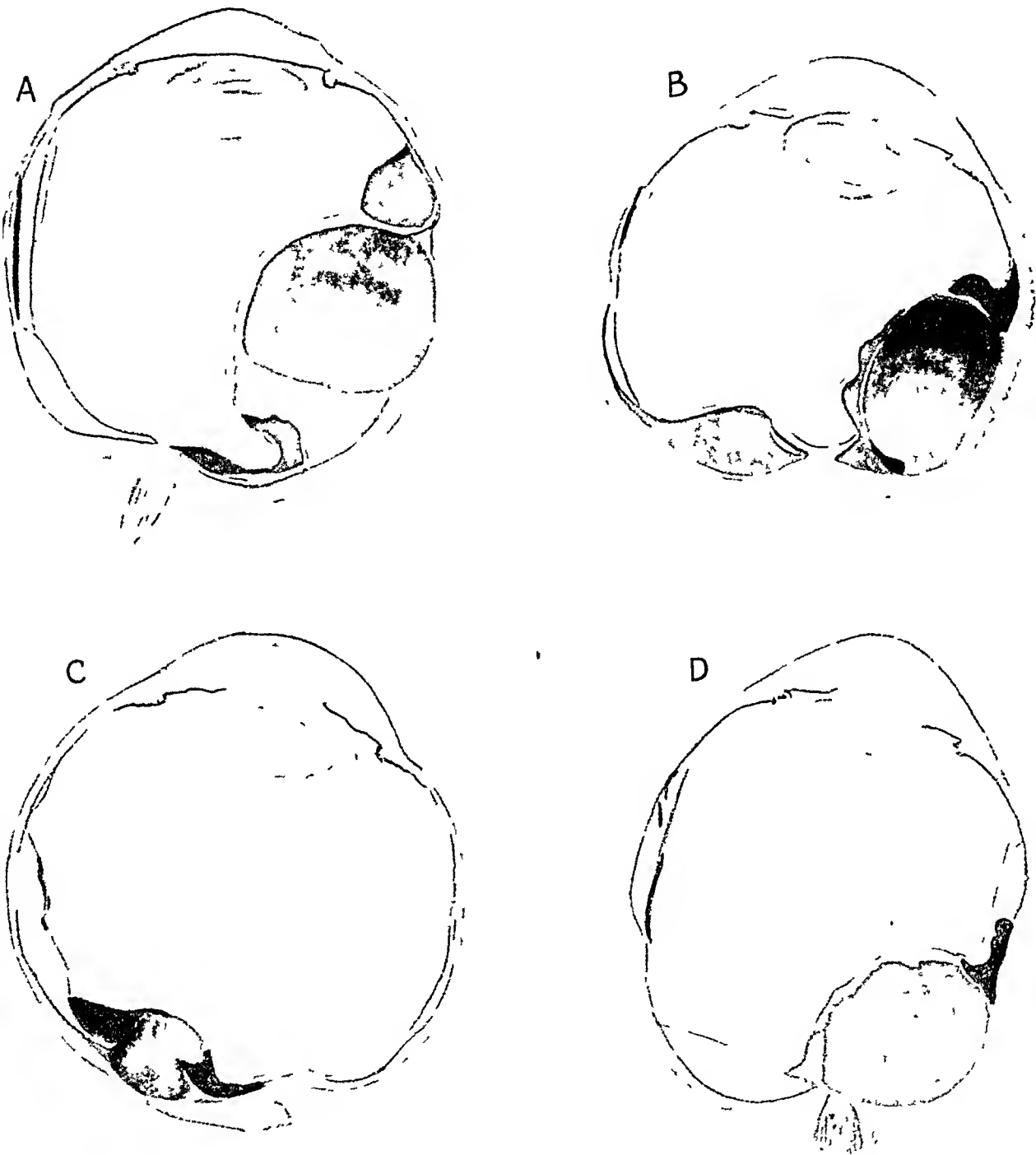


Fig. 4.—*A*, elongated, slitlike detachment opposite the ora serrata. *B*, slitlike detachment at the ora serrata, probably communicating with an extensive posterior detachment on the same side, opposite the tumor. *C*, slitlike detachment at the ora serrata, apparently independent, on the same side as the tumor. *D*, elongated, slitlike detachment at the ora serrata opposite the tumor.

No doubt the fluid was under a certain pressure. It is understandable that once it had reached a point at the ora serrata, where

most of the spontaneous and traumatic detachments occur, and where in infants' eyes the fold of Lange develops, the fluid gathered there and brought about the completed ring-shaped detachment at the ora serrata that was seen a number of times. There is little doubt that the disappearance of the rods and cones went hand in hand with the advance of the fluid and aided in the formation of the long narrow fissures between the pigment epithelium and the retina. There were cases in which the current in the fluid at the ora serrata appeared to have reversed itself and sent an extension posteriorly.

After all, from the anatomic standpoint, minimal retinal detachments and detachments at the ora serrata must represent steps in the progress of a sarcomatous separation of the retina the end of which is total detachment.

#### SOURCE OF THE FLUID

Since the subretinal fluid first attracts attention over a zone of immensely dilated and engorged blood vessels of the choroid at the base of the tumor, the most generally accepted theory is that the source of the fluid lies in this part of the choroid over which it first gathers. Here the choroid is many times the normal thickness. It is not unlikely that the tumor, the surface of which forms a part of the wall of the subretinal space, makes some contribution to the amount of fluid, particularly to the toxic element. At all events, the fact that the fluid, whether in a minimal retinal cavity or in a cavity in the ora serrata, took exactly the same stain as it did adjacent to the tumor speaks in favor of its being one continuous body. At distant points the choroidal vessels appeared not to be dilated, even under an area where the neuro-epithelial layers of the retina were most damaged. Surely the highly albuminous fluid in a tumor-shaped cavity at the ora serrata could not have come locally from the choroid and retina, which are here poorly supplied with blood. As the detachment progresses to completion, it may be that vessels of the choroid remote from the tumor add their share of fluid, the greater part of which would probably continue to come from the site of the tumor, which by its replacement of the stroma mechanically interferes with the normal circulation.

#### CLINICAL SIGNIFICANCE OF MINIMAL RETINAL DETACHMENTS AND DETACHMENT AT THE ORA SERRATA

The clinical recognition of minimal retinal detachment is difficult, particularly since there are no folds in the retina, the underlying fluid being too shallow to permit them to form. Indeed, this type of detachment might be referred to as the clinically "invisible type." However, the transparency of the retina may be so impaired as to cause the markings of the choroid to be indistinct. A reduction in

the field for blue corresponding to an area distant from the tumor should arouse suspicion of a minimal detachment.

With respect to the clinical recognition of detachment at the ora serrata, the extreme periphery of the retina is normally blind and is inaccessible with the ophthalmoscope unless the method of making pressure on the wall of the globe with the finger, as described by Trantas,<sup>5</sup> is employed. It is possible, however, that with careful search one may discover such a detachment, one that extends far back, using the indirect method of ophthalmoscopic examination. Finally, minimal detachments of the retina and those at the ora serrata clinically and anatomically would seem to be so characteristic of early sarcoma of the choroid as to be of pathognomonic importance.

57 West Fifty-Seventh Street.

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5. Trantas, A.: Moyen d'explorer par l'ophthalmoscope et par l'ophthalmoscope et par translucidité la parti antérieure du fond oculaire, le cercle ciliaire y compris, Arch. d'opht. 1900; Ophthalmoscopie du corps ciliaire, Gaz. med. d'orient.

## USE OF HYALURONIDASE WITH LOCAL ANESTHESIA IN OPHTHALMOLOGY

Preliminary Report

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THE ADVANTAGE of greater diffusion of an anesthetic solution for retrobulbar injection and nerve block is immediately apparent.

After Hoffman and Duran-Reynals<sup>1</sup> and McClean<sup>2</sup> reported the "spreading factor" of a substance found in the testes of normal rabbits, the use of this substance to increase the spread of anesthetic occurred to me. In 1936 I made a series of injections on rabbits to estimate the spread or diffusion of a solution of procaine hydrochloride with the addition of testicular extract. Ferric chloride was added to the solution to show the extent of diffusion when the tissues were sectioned and stained with Perles' stain. There was a marked increase in diffusion following injections in which testicular extract had been added to the anesthetic solution.

A subconjunctival injection of procaine hydrochloride with testicular extract was also given in one eye of a series of rabbits, and a control injection using procaine hydrochloride solution without testicular extract, in the other eye. The eyes were enucleated one, two and five minutes after the injection. The two eyes of a rabbit which had been enucleated five minutes after the injection were examined by Dr. A. B. Reese, who reported a much greater diffusion in the specimen in which the testicular extract had been added to the anesthetic solution. Although convinced that the testicular extract increased the diffusion of the anesthetic solution, the stimulation of cell growth in vitro by testicular extract, reported by Carrel,<sup>3</sup> and of Rous sarcoma (chicken tumor I), reported later by Hoffman, Parker and Walker,<sup>4</sup> suggested the possibility of undesirable side effects and discouraged its clinical use.

As the study of the mucopolysaccharides and mucolytic enzymes progressed, hyaluronidase was found to be the factor in testis responsible for the spreading. The enzyme hyaluronidase was first isolated

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1. Hoffman, D. C., and Duran-Reynals, F.: *J. Exper. Med.* **53**:387, 1931.

2. McClean, D.: *J. Path. & Bact.* **34**:459, 1931.

3. Carrel, A.: *J. Exper. & Med.* **17**:14, 1913.

4. Hoffman, D. C.; Parker, F., Jr., and Walker, T. T.: *Am. J. Path.* **7**:523, 1931.

by Meyer and associates<sup>5</sup> from patients with type II pneumonia. Later a wide distribution was reported by Meyer and associates<sup>6</sup> and also by Chain and Duthie.<sup>7</sup> Besides being present in micro-organisms, its occurrence in the animal body in extracts of spleen, testis, ciliary body and iris has been demonstrated.

According to Meyer,<sup>8</sup> the action of hyaluronidase depolymerizes and hydrolyzes hyaluronic acid, a mucopolysaccharide acid, which was first isolated by Meyer and Palmer<sup>9</sup> from bovine vitreous humor. Subsequently, Meyer and his co-workers found it in the human umbilical cord,<sup>10</sup> bovine aqueous and vitreous of pigs,<sup>11</sup> bovine and human synovial fluid,<sup>12</sup> mesenchymal tumors<sup>13</sup> and the skin of pigs.<sup>14</sup> In animal tissue hyaluronic acid seems to bind water in interstitial spaces and holds cells together in a jelly-like matrix which obstructs diffusion.

Chain and Duthie<sup>7</sup> also observed that the hyaluronidase activity of testicular extract was similar to the "spreading factor" reported earlier by Hoffman and Duran-Reynals<sup>1</sup> and McClean.<sup>2</sup> These studies established the fact that the addition of hyaluronidase caused a rapid dispersion of fluid when injected into tissues. The rapid dispersion is brought about by a depolymerization and hydrolysis of the hyaluronic acid gel. The reduction in viscosity removes one of the barriers to diffusion of fluid and allows it to permeate the tissues more rapidly and widely.

The clinical use of hyaluronidase, until comparatively recently, has not seemed practical, as it was not readily available in purified form. Now a highly purified hyaluronidase<sup>15</sup> is available, and observations on its use with local anesthetic procedures about the eye are presented in this paper.

One hundred and nine preoperative injections of an anesthetic solution containing hyaluronidase were given. The surgical procedures included minor operations on the lids, cataract extractions, enucleations with implants and operations for glaucoma, retinal detachments and strabismus.

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5. Meyer, K.; Dubos, R., and Smyth, E. M.: *Proc. Soc. Exper. Biol. & Med.* **34**:816, 1936; *J. Biol. Chem.* **118**:71, 1937.

6. Meyer, K.; Hobby, G. L.; Chaffee, E., and Dawson, M. H.: *J. Exper. Med.* **71**:137, 1940.

7. Chain, E., and Duthie, E. S.: *Nature, London* **144**:977, 1939.

8. Meyer, K.: *Physiol. Rev.* **27**:3 and 335, 1947.

9. Meyer, K., and Palmer, J. W.: *J. Biol. Chem.* **107**:629, 1934.

10. Meyer, K., and Palmer, J. W.: *J. Biol. Chem.* **114**:689, 1936.

11. Meyer, K., and Palmer, J. W.: *Am. J. Ophth.* **19**:859, 1936.

12. Meyer, K.; Smyth, E. M., and Dawson, M. H.: *J. Biol. Chem.* **128**:319, 1939.

13. Meyer, K., and Chaffee, E.: *J. Biol. Chem.* **133**:83, 1940.

14. Meyer, K., and Chaffee, E.: *J. Biol. Chem.* **138**:491, 1941.

15. Hydase® (lyophilized hyaluronidase) for this study was supplied by Wyeth Incorporated, Philadelphia.

The anesthetic solution used was procaine hydrochloride, 2 per cent. with potassium sulfate, 0.4 per cent. One drop of epinephrine hydrochloride (1:1,000) and 30 turbidity-reducing units of hyaluronidase (hydase®) were added to each 5 cc. of the anesthetic solution. Two more drops of epinephrine hydrochloride were added for cone injections if not contraindicated.

In order to have a more concentrated solution of epinephrine for injections into the muscle cone and to avoid using more than 3 drops of epinephrine hydrochloride the following procedure was used: In a 5 cc. syringe containing 6 cc. of anesthetic solution, 1 drop of epinephrine was added. The injection of the temporofacial nerve at the site recommended by O'Brien<sup>16</sup> was first given, using about 3 cc.; 2 more drops of epinephrine hydrochloride were then added to the remainder in the syringe before giving the cone injection.

Without the use of hyaluronidase, excellent superficial anesthesia for surgical procedures on the lid and for minor operations on the globe is produced by subcutaneous and subconjunctival injections of a procaine-epinephrine solution. However, with hyaluronidase added to the anesthetic solution, there is less ballooning of the tissues, owing to rapid diffusion, and not as much procaine solution is required to produce the anesthesia. Massage following the injections further increases diffusion.

Although it has been possible to produce akinesia of the orbicularis muscle since 1914 by the method of blocking the branches of the temporofacial nerves, as advocated by van Lint,<sup>17</sup> and, later, by the more proximal injection suggested by O'Brien,<sup>16</sup> some surgeons experience difficulty in obtaining complete paralysis of the orbicularis. The addition of hyaluronidase practically obviates this difficulty, so that a second injection is rarely necessary.

To prevent loss of vitreous and other serious complications, temporary paralysis of the extraocular muscles is probably second in importance to the paralysis of the orbicularis muscles. While this can be produced by orbital injections of a procaine-epinephrine solution, often there is still some activity of the superior rectus and other muscles. The action of these muscles can be partially controlled by means of bridal sutures, but temporary paralysis of all the extraocular muscles would be preferable. Hyaluronidase added to the anesthetic solution used in a retrobulbar or cone injection followed by massage, as previously described,<sup>18</sup> accomplishes this in a higher percentage of cases. Injections

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16. O'Brien, C. S.: *Tr. Sect. Ophth., A. M. A.*, 1927, p. 250.

17. van Lint, M.: *Ann. d'ocul.* **151**:420, 1914.

18. Atkinson, W. S.: *Local Anesthesia in Ophthalmology*, *Arch. Ophth.* **30**: 777 (Dec.) 1943; *Am. J. Ophth.* **31**:1607, 1948.

into the muscle cone of more than 1.5 cc. may be safely given for cataract extraction because the solution diffuses rapidly. A more complete anesthesia of the orbital contents and paralysis of the muscles are thus obtained, and any proptosis subsides quickly. For enucleation, 5 cc. or more may be injected.

Hypotony has been more pronounced after cone injections with hyaluronidase added to the anesthetic solution. In 20 eyes with a normal intraocular pressure averaging 19 mm. Schiøtz, the decrease in pressure ranged from 6 to 9 mm. of mercury five minutes after the injection was given. In 2 cases, the pressure was unchanged at the end of five minutes, but at the end of ten minutes it had dropped 7 mm. of mercury in one eye and 8 mm. in the other eye.

The hypotony appeared even more pronounced after the section, and after extraction of the cataractous lens the cornea occasionally collapsed. On raising the corneal flap, one could see the surface of the vitreous well back of the plane of the iris. With such extreme hypotony the usual method of applying the hook is not as effective. Consequently, the mechanics of the intracapsular extraction, as described by Harrington,<sup>19</sup> are changed. The extraction is slower and more difficult. However, with the eye soft, it seems fair to assume that vitreous is less likely to prolapse. Possibly a change in the method of applying pressure and in the ratio of pressure to traction will facilitate the extraction in the presence of marked hypotony.

Whether the extreme hypotony is due to a greater relaxation of the extraocular muscles, to a more extensive constriction of the arteries entering the globe or to the depolymerization and hydrolysis of the hyaluronic acid in the vitreous, causing water to be released, is difficult to determine. Possibly it is a combination of all three factors. In any case, the problem is an interesting one and deserves study. It seems of particular importance because in eyes with glaucoma there is a more striking drop in the intraocular pressure than occurs after a cone injection without hyaluronidase. In a case of absolute glaucoma, the pressure, which was over 90 mm. Schiøtz before the injection, had dropped to 55 mm. Schiøtz five minutes after the injection.

In order that I might have data on a larger group of cases to study, Dr. John H. Dunnington has followed the same procedure on a series of cases. He feels that it is too soon for him to form a definite opinion in regard to the value of hyaluronidase in anesthesia. However, in a recent letter, he stated that the substance seemed to be of great help in producing akinesia and hypotony for cataract extractions.

My impression is that anesthesia is produced more rapidly when hyaluronidase is added to the anesthetic solution and that the duration

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19. Harrington, D. O.: *Tr. Am. Ophth. Soc.* 46:294, 1948.



of anesthesia is about the same as without it. Epinephrine was used in the anesthetic solution for all the injections. Kirby and associates<sup>20</sup> reported the duration of anesthesia to be about the same when epinephrine hydrochloride was added to the anesthetic solution of procaine hydrochloride with hyaluronidase but that it is shorter without the epinephrine. Another interesting observation of theirs was that "the degree of spread was greater when epinephrine was added to the procaine-hyaluronidase solution." This was attributed to the slower absorption due to the epinephrine.

For corneoscleral trephining in cases of glaucoma, a cone injection of procaine hydrochloride and epinephrine may lower the intraocular pressure to such a degree that the iris does not prolapse. The addition of hyaluronidase lowers it still further; so, unless a lower pressure is desired, a cone injection with or without hyaluronidase is contraindicated.

After an intradermal injection to produce a wheal, the site was at first ischemic, but the area of ischemia quickly disappeared and was followed by a corresponding area of erythema. Several minutes after a cone injection in which hyaluronidase had been added to the anesthetic solution, the conjunctival and episcleral vessels frequently filled with blood so that the eye was red even though it had previously been blanched with phenylephrine (neo-synephrine®), which had been used to dilate the pupil. No effect on the pupil attributable to the hyaluronidase was observed. The action of tetracaine (pontocaine®) hydrochloride as used for instillation anesthesia did not appear to be influenced by the addition of hyaluronidase.

#### SUMMARY

With the addition of hyaluronidase to injections of an anesthetic solution of procaine and epinephrine, the following observations were made:

1. There was a greater diffusion of the anesthetic solution.
2. Anesthesia occurred more rapidly than that induced by a solution without hyaluronidase, and the duration was about the same.
3. There was less ballooning of the tissues, and the area of anesthesia was greater.
4. More effective akinesia of the orbicularis and extraocular muscles was obtained.
5. Hypotony was pronounced after cone injections and was occasionally sufficient to make the cataract extraction more difficult but safer, with vitreous less likely to present.

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20. Kirby, C. K.; Eckenhoff, J. E., and Looby, J. P.: *Surgery* **25**:1 and 101, 1949.

6. Ischemia due to epinephrine was quickly followed by erythema, which was also of brief duration.

7. The eye frequently became red after a cone injection. .

#### CONCLUSION

The addition of hyaluronidase to procaine-epinephrine solution enhances anesthesia and merits further study.

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## SHORTENING OF THE EYEBALL FOR DETACHED RETINA

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IN 1931 I began to operate for retinal detachments which seemed otherwise incurable by shortening the eyeball. The technic of this operation was published in 1933.<sup>1</sup> In the United States, Pischel described this operation in the ARCHIVES in 1939.<sup>2</sup>

In this paper I wish to describe those details of the operation which I have changed since my first publication, enumerate the present indications for this operation and, finally, present the results. A detailed description of the operation appeared in "Ophthalmologische Operationslehre," edited by Thiel.<sup>3</sup>

If one shortens an eyeball, one diminishes its volume, and therefore an adequate amount of fluid must be drained from the eyeball during the operation. Prior to the time of the first publication, I tried to drain the eye by puncturing the exposed choroid with a discission needle (case 1). I did this using the Zeiss binocular magnifying lens and carefully avoiding any injury to the blood vessels. This type of drainage works well in cases of detachment in which the vitreous is so far detached posteriorly that the puncture hits the subvitreal space. This condition is met sometimes in aphakic eyes, especially in young persons. On the other hand, soon after performing this operation, my colleagues and I encountered cases in which the puncture of the exposed choroid released a little subretinal fluid and then the outflow stopped, because the retina became reattached. Then puncture of the attached retina led again to drainage, or the opening became closed by solid vitreous. In the latter case we perforated by coagulation more posteriorly, or we punctured the anterior chamber and opened the puncture opening repeatedly so that we could continue the shortening operation. In 1 of these cases the solid vitreous produced dilation of the needle opening in the choroid and retina and a solid prolapse appeared. I cut the prolapsing vitreous away, and a new mass of solid prolapse appeared, which I cut away again and again in order to lessen the volume of the eyeball and

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1. Lindner, K.: Heilungsversuche bei prognostisch ungünstigen Fällen von Netzhautabhebung, *Ztschr. f. Augenh.* **81**:277, 1934.

2. Pischel, D. K., and Miller, M.: Retinal Detachment Cured by Eye-Ball Shortening Operations: Report of a Case, *Arch. Ophth.* **22**:974 (Dec.) 1939.

3. Thiel, R.: *Ophthalmologische Operationslehre*, Leipzig, Georg Thieme, 1943, vol. 2.

complete the shortening operation. But the retina of the other side was pulled toward the choroidal opening by the adherent solid vitreous, and the eye was lost.

Since this unfavorable result we have given up the puncturing of the exposed choroid, and we drain the eye only by perforating coagulations placed posterior to the detached vitreous. In shortening of the superior half of the eyeball, the perforating coagulations not only should drain the eye but should help to reattach a detached retina or to fasten an attached retina in place. When this drainage was arrested by the reattachment of the retina, we made a puncture again in the same place. If this did not help we made punctures more posteriorly or opened the anterior chamber and reopened the wound as often as necessary.

Hence, our present procedure is as follows: First, we must know the condition of the vitreous. The best way to examine the vitreous is with the slit lamp of Goldmann, in which the observation system and focused slit are moved together and are fitted, in addition, with the lens of Hruby and with his fixation lamp.<sup>4</sup> We must know how far the vitreous is detached posteriorly. For instance, if there is a flat posterior detachment, the strip to be excised should not be wider than 2 mm., for in cases of this type the eye is drained chiefly by puncturing the anterior chamber. From the anterior chamber we cannot remove sufficient fluid to allow the excision of a strip 3 mm. or more in width. However, in cases with the vitreous detachment far in front strips up to 6 mm. or more in width can be excised (case 5). Traction on the strands in the vitreous must be noted carefully, since they influence the method of operating (case 3).

We perform all shortening operations with local anesthesia. Our patients are tried for sensitivity to cocaine by injecting 1 cc. of a 1 per cent solution of cocaine subcutaneously. At the operation we inject a mixture of equal parts of 3 per cent cocaine and 2 per cent procaine hydrochloride. We add the 1:10,000 solution of ephinephrine hydrochloride in sufficient quantity to make it equal to one tenth of the total volume of the mixture. We use from 0.5 to 2 cc of this mixture. Sometimes in the case of elderly patients I have made several radial conjunctival incisions instead of a single circular one, to keep the cornea under better nutritional condition, although we never had complications due to insufficiency in this respect. The technic of incision of the sclera and of insertion of the sutures is the same as that which was described originally. Since 1945 we have used silk sutures and operate with cotton gloves. We had no sterile surgical gut. I emphasize the importance

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4. Hruby, K.: Ueber eine wesentliche Vereinfachung der Untersuchung des hinteren Augenabschnittes im Lichtbüschel der Spaltlampe, *Arch. f. Ophth.* **143**:224, 1941; *ibid. Klin. Monatsbl. f. Augenh.* **108**:195, 1942.

of very sharp needles for suturing the sclera. I have found only those of Grieshaber (Schaffhausen, Switzerland) satisfactory. Not only is it difficult to operate with dull needles, but it is dangerous to the eye. Especially in areas which had been coagulated before the softened sclera may rupture from rough handling when dull needles are used. The sutures should be inserted outside coagulated areas in the sclera, because the latter do not give enough support to the sutures. In some cases I have excised the whole coagulated area. Therefore in all cases of detachment we observe the rule of coagulating as near the circumference of the holes as possible, if we choose this operative procedure.

The incision through the sclera at the beginning of the operation should be made before the eye is drained because of the difficulty of a through and through incision in the sclera in a soft eye.

I coagulate first with a blunt electrode and then use a perforating one inside the coagulated area to avoid hemorrhage. In some cases I insert Safar's double pins into the previously coagulated areas. The perforating needles must be 1.8 or 2 mm. long, for coagulated sclera is thicker than normal sclera. Then I begin the excision of the scleral strip at the place where the incision had already been carried down to the choroid. I expose no more choroid than an area which corresponds to one suture interval, so as to avoid the danger of rupture of the exposed choroid.

If the drainage stops, the retina most probably has become reattached in the perforated area. Then the retina must be perforated at the site of the electrocoagulation. If this is not followed by drainage, the perforation is made farther posteriorly, or the anterior chamber is punctured; for this purpose, the keratome of Wessely is used; an incision is made under a conjunctival flap, and the incision is reopened from time to time with a spatula. It may be necessary to wait several minutes before the anterior chamber refills with fluid and another puncture is made.

The greatest danger in this operation is that of an intraocular hemorrhage. It should be prevented by all means. Vortex veins must be avoided; if necessary, the scleral part where a vortex vein may be encountered is avoided (cases 1 and 2; shortening). If, with the strip, the scar of a former shortening (case 3, operation 4; case 4, shortening 2; case 5, shortening 2 and 3) is excised, the choroid is often found to be adherent to the area of the scar and must be carefully separated with a blunt spatula, just as when coagulated areas are excised. When an intraocular hemorrhage develops at operation, the eye is lost.

In several cases I tried to shorten the eyeball by folding a surgically thinned sclera instead of excising it in its whole thickness. However, after some initially good results, the condition in these cases became

worse. Therefore I have given up this method, since the folded sclera unfolded again when the stitches were absorbed (case 3). The technic to be described would have been less dangerous and much easier to perform than the excision. In some cases severe edema of the conjunctiva from lymphatic stasis developed a few days after the operation. Daily massage of the conjunctiva with a glass rod is necessary. In doing this we had no complications in the cornea. After this operation patients are kept in bed only four to five days.

We consider the following types of retinal detachment suitable for this operation:

1. Aphakic eyes without detectable holes. In such cases the vitreous is detached far forward (case 1).

2. Aphakic eyes in which operation had been performed for retinal holes without success (case 2).

3. Detachment with the retina fixed by strands in such a way that for mechanical reasons a reattachment was not possible (case 3).

4. Detachment operated on several times by the usual methods for which there is no hope of improving the condition by further surgical treatment of the same kind (cases 4 and 5).

What part of the eye should be shortened, and how often can an eye be shortened?

One can shorten an eyeball all around in one session.<sup>1</sup> I performed such an operation once without complications. However, the local anesthesia did not last long enough for me to complete the operation without pain in spite of repeated injections during the operation. Only general anesthesia, as used in the United States, would permit this long-lasting operation, in which I had to make radiating conjunctival incisions and a temporary resection of the internal rectus muscle. Therefore, I shorten only half the eyeball in one operation. The operation on the second half may be undertaken after an interval of three weeks.

If there was no binocular vision prior to the detachment, I shorten the upper half first. The operation on the lower half may follow, if necessary. Our aim is to reattach the upper half of the retina or to secure the reattachment of this portion of the retina because of the greater importance of the lower visual field. Perforating coagulations through the attached retina will keep this part of the retina in place later. In monocular cases the superior rectus is not reattached. On the contrary, I place a suture in the superior rectus, divide it, pull it away out and excise a piece of muscle. The remaining muscle slips back into the orbit. The same procedure is followed if the lower part of the eye is being shortened. In this way we lessen the dangerous vertical move-

ments of the eye. A remaining detachment in the lower part would not be influenced by lateral movements of the eye. The two oblique muscles are left uncut so as to preserve vertical mobility (Bell's movement to protect the cornea).

In eyes with vitreous strands preventing a reattachment, the scleral excision should be correctly placed to avoid the deleterious effect of traction by the strands. When coagulated areas are present, the surgeon may be forced to excise them or to operate in a different area.

In cases in which there was previous binocular vision and the other eye is intact, we prefer the shortening of the nasal side at the first operation. This has no influence on the vertical position of the eye. Slight horizontal deviations do not play such a disturbing role as do vertical deviations. After each shortening the eyeball becomes less mobile; it is preferable, therefore, to start with the more difficult (nasal) side. The operation on the temporal side may follow. If in such a case, for some special reason, the shortening of the upper or the lower half of the eye is desirable, I reattach the muscle as far back of its insertion as the strip is wide. But the muscle must always be reattached on the corneal side of the excised area; otherwise the wound would be opened. This detail should be considered in determining the placing of the excision.

Shortening operations were repeated several times in many cases in order to secure partial or total reattachment of the retina. The shortening operation may be considered as a race between the shrinking vitreous and the decrease in the size of the eye, which may continue for years (cases 1, 2 and 5). This race is lost if an intraocular hemorrhage takes place during the operation.

Twice I tried to excise radial strips of sclera with the idea of lengthening a hypermetropic eye rather than of shortening it. Besides, this technic may relieve the pull of the equatorially stretched vitreous. This technic did not work, as the choroid may fold on account of traction of the vortex veins. In circular excisions the choroid adapts itself easily to the shortened sclera.

To give an idea of the painstaking work connected with this difficult operation and the length of time it takes to obtain a satisfactory result, I submit several cases illustrating the various problems.

#### REPORT OF CASES

CASE 1.—Peter D., aged 29, had an operation for perinuclear cataract in 1938. This was soon followed by retinal detachment. Bed rest was prescribed and a compressing bandage was worn for a longer period. In April 1940 vision was very poor. The first examination, on Oct. 16, 1940, revealed that the left eye was blind, due to glaucoma and that in the right eye there was secondary cataract with

a very small hole in the secondary membrane. The retina showed a bullous detachment below and a flat detachment above; no hole was visible. Vision was limited to counting fingers, eccentric.

October 23, First Shortening (fig. 1 *A*): A strip 2 mm. wide from the upper half of the globe was excised. A suture was passed through the superior rectus, the muscle was pulled forward and a long piece of muscle was resected. The muscle was then allowed to slip back into the orbit. The exposed choroid was punctured in two places. The first puncture hole drained well. The second perforation showed a small pearl of solid vitreous. Therefore perforating coagulations were made temporally above. Owing to pressure, the vitreous pearl burst and some fluid escaped.

December 19: Vision with a + 12.00 D. sphere was 2/60. The retina was detached below.

December 21, Shortening of Lower Half (fig. 1 *B*): The inferior rectus was resected, with excision of a piece of muscle. A 2 mm. strip of sclera was removed.

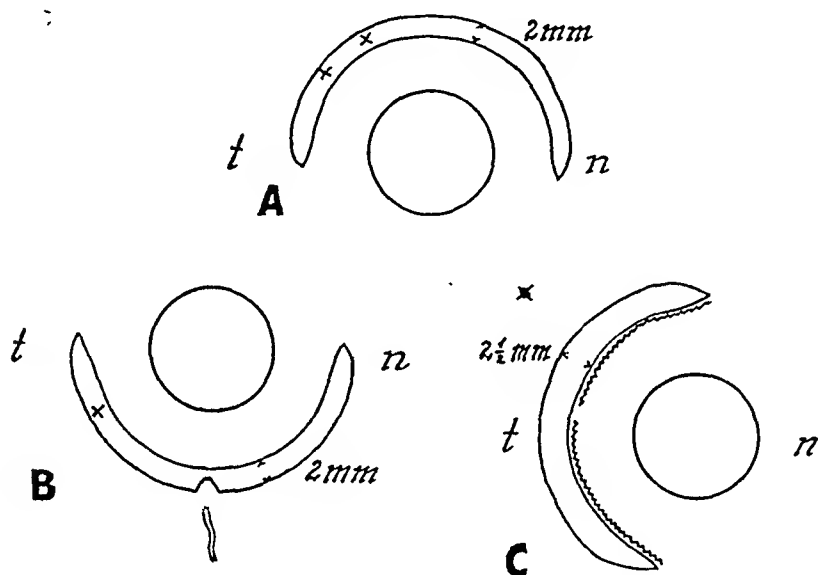


Fig. 1 (case 1).—*A*, Oct. 23, 1940; *B*, Dec. 21, 1940; *C*, Nov. 27, 1941.

One puncture of the exposed choroid provided sufficient drainage. A small piece of sclera was left because of the presence of a vortex vein.

Feb. 2, 1941: With a + 20.00 sphere vision was 6/36. There was a detachment below.

November 11: With + 20.00 D. sphere vision was 1/60. There was a detachment below.

Nov. 27, 1941, Shortening of the Outer Half (fig. 1 *C*): The excision of a strip 2.5 mm. in width was performed behind the hardly visible scar of the former shortening operations. One perforating coagulation placed temporally and above provided sufficient drainage.

December 12: Vision was 6/36 with a + 21.00 sphere.

Feb. 10, 1942: With a + 20.00 sphere vision was 6/18. The lower part of the retina was detached. The retina became entirely reattached and remained so, but the function of the lower part of the retina did not return.

Jan. 21, 1943: With a + 21.00 sphere vision was 6/24.

March 28, 1944: With a + 20.00 sphere vision was 6/18. The retina was totally attached. A third of the upper field was defective.



On last examination, on May 5, 1948, vision with a  $+ 21.00$  sphere was 6/24. The field was unchanged; the retina was attached.

The patient has been able to study and is now a teacher in a high school.

CASE 2.—Michel T., aged 32, from Sofia, Bulgaria, was referred by Dr. Levieff, with typical Marfan's disease. The right eye had had a total detachment of the retina for four years, of unknown cause. Operation had been performed three times, without result. Vision was equal to perception of hand movements at 1.25 meters. Detachment appeared in the left eye in September 1941.

Examination on Oct. 9, 1941 revealed slight hydrophthalmos, iridodonesis and a shrunken lens floating in the lower half of the vitreous. A small retinal hole lay temporally and above.

Oct. 15, 1941, First Operation: Coagulations were made around the hole, without result.

November 4: The operation was repeated. The macula became attached; the retina in the temporal periphery was slightly detached.

Dec. 2, 1941: Vision with correction was 6/8.

February 1942: The retina, including the macula, was detached in the lower half; no hole was visible; vision was reduced to 6/36.

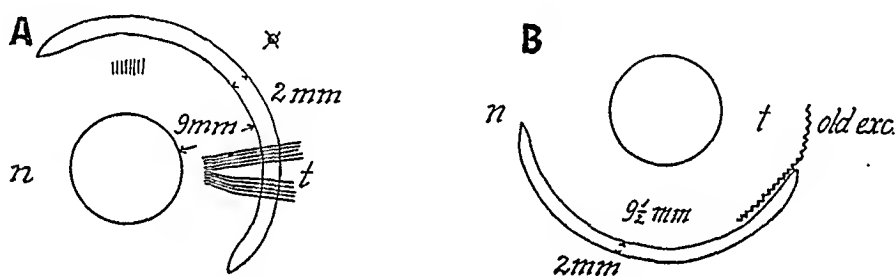


Fig. 2 (case 2).—A, Feb. 20, 1942; B, Aug. 25, 1942.

Feb. 20, 1942, First Shortening (fig. 2 A): A strip 2 mm. wide extending from the upper nasal to the lower temporal quadrant, was excised. The superior rectus was temporarily divided. The external rectus was tenotomized to facilitate the shortening beneath the muscle. One perforating coagulation was performed above and temporally; this had to be reopened again, as the drainage had stopped.

April 1, 1942: Vision with correction was 6/18?

Aug. 13, 1942: Vision was much poorer; with a  $+ 12.00$  sphere it was 2/36.

Aug. 25, 1942, Second Shortening (fig. 2 B): A strip 2.5 mm. wide was excised in the lower half. No note on the effect of the perforating coagulation was made.

Oct. 15, 1942: Vision with a  $+ 8.00$  sphere was 6/18. The retina below was slightly detached.

April 23, 1943: Vision was again reduced, being limited to counting fingers at 6 meters. The lower half of the retina, including the macula, was detached.

A careful search at this time revealed two small holes quite peripherally at the 10:30 meridian.

May 5, 1943: The holes were sealed by several coagulations.

June 29, 1943: Vision with correction was 6/12. A small area of retina was detached in the lower periphery. The field for red was contracted above; the field for movements was normal.

The patient used stenopeic spectacles until January 1947. A line of demarcation developed at the border of the remaining detachment. The patient was not cured, but he considers that his eye has healed and he lives a normal life.

CASE 3.—Ivan, A., aged 13, from Sofia, Bulgaria, who was referred by Dr. Balabanova, had been struck five years before by a piece of wood in the left eye and the eye had become blind. Three months before I saw him a similar injury occurred to the right eye.

Examination revealed total detachment, especially temporally, with flat detachment of the macula. From the disk strands extended toward the temporal portion of the retina (after hemorrhage?), where they were attached. No hole was visible.

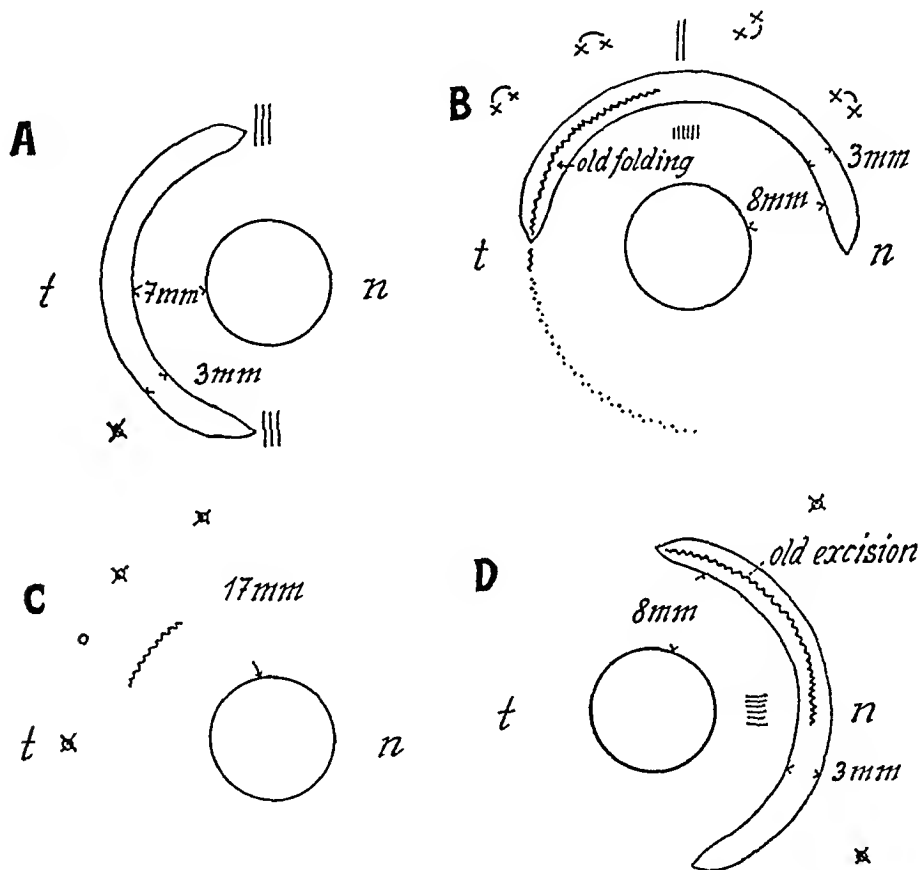


Fig. 3 (case 3).—A, Nov. 4, 1946; B, May 31, 1947; C, June 24, 1947; D, July 27, 1947.

There was a detachment of the vitreous in front of the retina at a distance which was comparable to the thickness of the lens. Vision was limited to counting fingers at 1.5 meters.

As reattachment of the retina seemed impossible on account of the strands and as no hole could be found, I had the idea of folding the sclera after thinning it and of approximating the inflamed choroid to the immobilized retina.

Nov. 4, 1946, Shortening of the Eye by Folding (fig. 3A): The sclera was thinned along a strip of 3 mm. This scleral membrane was then touched with 3 per cent potassium hydroxide to produce inflammatory changes in the choroid. The normal edges of the scleral wound were sutured together. One perforating coagulation was done, temporally and below.

June 16, 1946: Vision with — 8.00 sphere was 3/24. In the extreme periphery a protruding scleral fold was visible. The retina seemed to be in contact with the choroid.

May 1947: The detachment was again visible. The scleral wall had disappeared; the detachment was unchanged, and no hole was visible.

May 31, 1947, Shortening Operation (fig. 3 *B*): The upper half of the eye was shortened in the usual way by excision of a strip 3 mm. wide. The scleral fold had totally disappeared; the sclera was stretched smooth, and the former thinned sclera had normal thickness. Hence, the folding operation was of no lasting effect.

June 24 (fig. 3 *C*): The retina remained detached in the temporal half. To bring it into contact with the choroid, I made four trephinations in the temporal half and touched the exposed choroid with 4 per cent potassium hydroxide; then I perforated three, the fourth was bleeding and was therefore not perforated. There was no change.

June 27, Shortening (fig. 3 *D*): I excised a strip 3 mm. wide in the nasal half. Two perforating coagulations were made nasally above and nasally below.

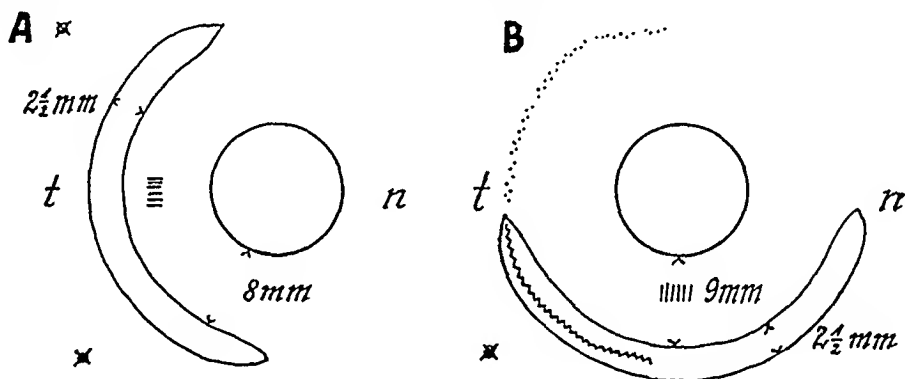


Fig. 4 (case 4).—*A*, June 4, 1944; *B*, June 14, 1944.

The retina was reattached. Vision with a — 10.00 sphere was 6/36. The field was normal at last examination, by Dr. Balabanova, in June 1948.

CASE 4.—Ruth H., aged 25, became blind in her left eye as a result of uveitis in her ninth year. Iritis occurred in the right eye in 1940. The eye healed in a short time. In September 1943 there was disturbance of vision after a fall, and on October 1943 the diagnosis was detachment, with a flap hole temporally and above. Three electrocoagulations were performed.

On the first examination, May 29, 1944, a bullous detachment was found everywhere except in the area of operation, temporally and above. In this area there were old choroidal patches. The vitreous was detached half way, with a single prolongation behind the detachment line. Vision was reduced to light perception. No hole was visible.

June 5, 1944, Shortening Operation in Temporal Half (fig. 4 *A*): A strip 2.5 mm. wide was excised from 6.30 to 11 o'clock, with two perforating coagulations. The first, temporally and above, did not fistulate, but the second, temporally and below, fistulated well.

June 14, 1944: The detachment became flat in the middle part. Vision with — 6.00 sphere was 2/36.

June 24, 1944, Shortening Operation (fig. 4B): A strip 2.5 mm. wide comprising the lower half was excised; this included the scar of the former shortening. One perforating coagulation temporally and below fistulated well. The retinal detachment became very flat on the temporal side. Far in the periphery two single holes were discovered at 9 and 10 o'clock (Dr. Heinz).

June 22, 1944: Closure of the two holes was made with four coagulations. The retina became totally reattached.

July 26, 1944: Vision was 6/36 with a — 3.00 sphere.

Vision gradually improved. At the last examination (1947), by Dr. Marchesani (Hamburg), vision with correction was 6/18.

In this case the retinal holes were visible only after the second shortening.

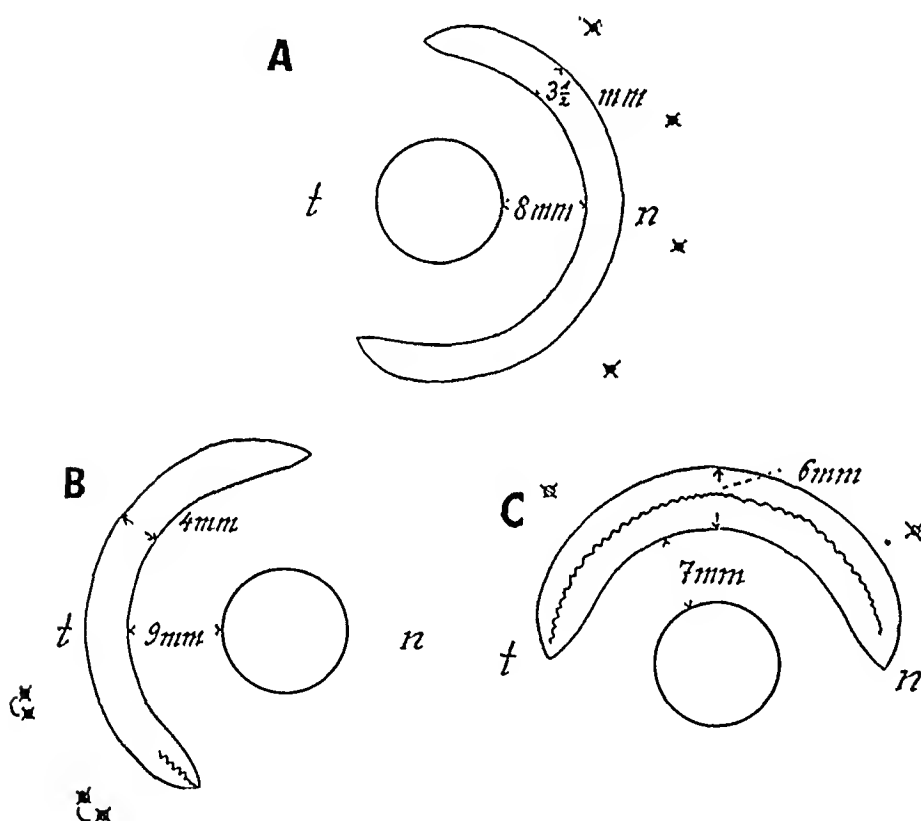


Fig. 5 (case 5).—A, May 4, 1946; B, Dec. 20, 1946; C, Nov. 15, 1947.

CASE 5.—Agnes D., aged 24, had a retinal detachment in the left eye which had appeared one year before. There was a high myopia of — 20 D. Peripheral holes were present temporally and below. Cure was effected by one operation on Aug. 20, 1946. With a — 25.00 sphere vision was 6/60. Degenerative changes were present in the macula. Detachment for one week had been present in the right eye.

June 17, 1946: Examination revealed a nearly complete detachment. There were a large peripheral tear in the retina and a single hole temporally and below. Vision with a correction of — 15 sph. — 2 cyl. was 3/36 —.

Two operations. on June 25 and July 23, 1946, in the neighborhood of the holes failed to affect the detachment. There was a bullous detachment; no hole was to be found.

May 5, 1946, Shortening Operation (fig. 5A): A strip 3.5 mm. wide was excised from 12 to 7 o'clock. Four perforating coagulations were made posterior to the excised area. The lower half of the retina remained detached, including the macula.

Dec. 20, 1946, Shortening Operation (fig. 5B): A strip 4 mm. wide was excised from 6:30 to 12 o'clock. It was difficult to apply the sutures in the area of former coagulations. The scar which resulted from the former shortening was excised. Two double pins of Safar were inserted, and good fistulation resulted.

Jan. 7, 1947: The retina was nearly attached. Vision with a — 14.00 sphere was 2/36. After a short time the detachment became more extensive.

Dec. 15, 1947, Shortening of the Upper Half (fig. 5C): The old shortening scars were excised in a strip 6 mm. wide. The first perforating coagulation, temporally and above, did not fistulate. The second, nasal and above, fistulated for some time, but then the outflow stopped. The anterior chamber was punctured, and the wound reopened several times.

Jan. 16, 1948: The retina was slightly detached, nasally and down; the macula was attached. Vision with — 10.00 sphere was 6/60. The macula was degenerated.

May 13, 1948 (Last Examination): Vision with a — 10.00 sphere was 6/60. The retina showed a flat detachment below; the macula was attached. There was slight enophthalmos. The field for hand movements was nearly normal, and there is a small field for blue. If the detachment increases again and includes the macula, a fourth shortening should be performed.

#### COMMENT

In describing these few cases, I feel like an oculist who mentions good cases of corneal transplantation and omits those in which the operation was harmful. Therefore I shall add the results of a statistical study of two years (1944 and 1945), which will be published later in detail.

During these two years, the shortening operation has been performed on 36 eyes at this clinic. At the time of the patients' discharge from the hospital 6 eyes were cured; 10 were improved; the condition of 9 was unchanged, and that of 11 was worse. Twenty eyes have been shortened once; 12, twice, and 4, three times. On account of the war and the present political conditions, only a part of the patients could be reexamined two or three years later. Four of the 6 cured patients were reexamined and had remained cured; the others (foreigners) did not return or answer letters. But 2 other patients, not cured before, came back with reattached retinas. The majority of the patients who were not cured and whom we could reexamine had become worse. For instance, 2 patients with but one eye who left the clinic with a small area of detachment and with fairly good vision came back with a total detachment. Hence, patients not completely cured should remain under observation for years (cases 1, 2 and 5), as initial improvement may be lost. As a rule, only patients with but one eye are willing to cooperate in this way. However, sometimes they cannot continue to stay under

observation because of the expense, especially in the case of foreigners. We instruct these patients to return at once if the condition of the eye should become worse.

If the upper part of the retina remains attached, the preservation of the lower field and the prevention of complicated cataract, or of other unfavorable sequelae, would qualify even a single operation as serving its purpose. One should not forget that all these eyes were considered practically lost and would have become worse.

In several of the eyes which were cured the improvement of function was slow. As a rule, when the retina had been detached for a long time, one year is required for the final functional result.

The shortening of the globe is a difficult and a tiring operation. But the patients with but one eye whom we save from total blindness (cases 1, 2, 3 and 4) repay us for the unsuccessful operations.

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# BILATERAL TOTAL OPHTHALMOPLEGIA WITH ADENOMA OF THE PITUITARY GLAND

Report of Two Cases; an Anatomic Study

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THE DIAGNOSIS of adenoma of the pituitary gland usually is made on the basis of one or more of three signs: changes in vision and visual fields, alterations in the sella turcica as demonstrated in roentgenograms and evidences of dyspituitarism. Until relatively recently cranial nerve palsies have not received the consideration they merit. During 1940 two noteworthy papers appeared, and they merit particular attention in this regard. Weinberger, Adler and Grant,<sup>1</sup> after reviewing 169 case records of verified adenomas of the pituitary gland, selected 14 cases which exemplified involvement of the cavernous sinus; they stated that these 14 cases by no means represented the total incidence of palsies of the cranial nerves within the cavernous sinuses in the cases they studied. Jefferson<sup>2</sup> described the symptomatology associated with extrasellar extensions of pituitary adenomas. A further communication containing detailed descriptions already available in these two papers would be superfluous. However, in neither of these papers or in the English literature, so far as I am aware, has there been mention of bilateral total ophthalmoplegia associated with pituitary tumor. During the past year I have observed a case of such a condition (courtesy of Dr. H. G. Johnson) and have notes on a second case which was identical as regards the ophthalmoplegia (courtesy, Dr. J. G. Arnold Jr.). A report of these cases is the primary purpose of this paper. An effort is also made to further understanding of the signs of pituitary tumor without restating what has been described authoritatively in the two papers selected for particular mention.

This paper contains (1) the findings in summary form in 50 consecutive cases of verified pituitary tumor seen in the Johns Hopkins Hospital; (2) a brief report of 2 cases of bilateral ophthalmoplegia (in this section two figures taken from Jefferson's paper<sup>2</sup> are included;

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From the Wilmer Ophthalmological Institute of the Johns Hopkins Hospital.

1. Weinberger, L. M.; Adler, F. H., and Grant, F. C.: Primary Pituitary Adenoma and the Syndrome of the Cavernous Sinus: A Clinical and Anatomic Study, *Arch. Ophth.* **24**:1197-1236 (Dec.) 1940.

2. Jefferson, G.: Extrasellar Extension of Pituitary Adenomas, *Proc. Roy. Soc. Med.* **33**:433-458, 1940.

they explain the mechanics of the sudden loss of vision which occurred in case 2); (3) a diagram which illustrates the possible routes of spread of adenoma of the pituitary gland; (4) a drawing of the cavernous sinus, and (5) comments on involvement of the fifth nerve as part of the syndrome of the cavernous sinus, as well as on loss of the corneal reflex.

#### FINDINGS IN FIFTY CONSECUTIVE VERIFIED CASES OF PITUITARY TUMOR

The frequency with which cranial nerve palsies and other signs occur with pituitary tumor is indicated in the following tabulation:

Types of Tumor:	No. of Cases	Percentage
Adenoma, 46; carcinoma, 4		
Loss of vision or changes in the visual fields.....	49	98
Dyspituitarism (loss of libido; amenorrhea; acromegaly).....	17	34
	9	18
Diplopia, history of; absence of manifest palsy.....	16	32
Paralysis of ocular muscles, one or more (including 2 cases of bilateral ophthalmoplegia).....	6	12
Third nerve.....	5	10
Fourth nerve.....	2	4
Fifth nerve (loss of corneal sensation).....	1	2
Sixth nerve.....	3	6
Nystagmoid movements.....	2	4
Proptosis .....	2	4
Papilledema .....	4	8
Involvement of frontal lobe.....	2	4
Involvement of temporal lobe.....	1	2
Pressure on brain stem and cerebellum.....	1	2
Spread into sphenoid sinus and nasopharynx.....	1	2
Cerebrospinal rhinorrhea.....	1	2
First Symptoms or Signs in Series		
Loss of vision.....	26	52
Acromegaly .....	8	16
Headache .....	7	14
Cessation of menses; loss of libido.....	7	14
Diplopia .....	3	6
Involvement of fifth nerve.....	0	0

*Comment.*—This series is small and consequently is not statistically of value. The incidence of carcinoma of the pituitary gland is unusually high. Also, loss of vision or changes in the visual fields occurred in this series of cases oftener than in other series of verified cases. The frequency of diplopia is in accord with what has been described by Cushing<sup>3</sup> and the observers already mentioned. It is undoubtedly true that if careful inquiry were made in every case of pituitary tumor it would be found that in about half the cases diplopia had been present at some time.

#### REPORT OF TWO CASES

CASE 1.—J. A., a man aged 51, had exhibited evidences of acromegaly for twenty years. He suddenly experienced excruciating pains in the head and face and within a few hours exhibited bilateral total ophthalmoplegia. There was no demonstrable involvement of the fifth nerve; the corneal sensitivity remained

3. Cushing, H.: *The Pituitary Body and Its Disorders*, Philadelphia, J. B. Lippincott Company, 1912.



normal in both eyes. Roentgenograms revealed enlargement of the sella turcica with erosion. Visual acuity could not be tested accurately but was approximately 20/70 and 10/200 in the right and left eyes, respectively. There were incomplete bitemporal field defects. Operation was followed, after a stormy course, by complete recovery from ophthalmoplegia and return of vision to normal levels; the fields became normal.

Twenty-five years before examination at this clinic, evidence of acromegaly—enlargement of the feet, hands and head—first made its appearance. Ten years later the patient noticed gradual enlargement of the tongue. For five years he had complained of fatigability and some loss of libido. Six months before his admission there was blurring of vision of the left eye. Two weeks before admission he complained of nausea, vomiting and generalized headache. The vomiting and headaches continued for two days, during which he noted further failure of vision and inability to open his eyes. At the end of two days he was unable to open either eye.

He showed the characteristic changes of acromegaly in the face, feet and hands, and a large tongue. The skin was soft and sallow. There was normal growth of beard but no axillary and a small amount of pubic hair.

There was complete bilateral paralysis of the third, fourth and sixth nerves. The corneal reflexes were normal. The pupils were dilated and fixed to light. There was moderate pallor of the optic disks with visual acuity of 20/70 and 10/200, respectively, for the right and left eyes. There was a defect in both temporal fields. The neurologic examination was otherwise without significance.

The usual laboratory tests yielded normal results. Roentgenograms revealed typical changes of acromegaly in the hands and feet. The sella turcica was ballooned. An electroencephalogram showed no significant abnormalities.

On Oct. 1, 1948 a transfrontal operation was performed on the left side. The left optic nerve was pushed forward by a large white-yellow mass which extended between the two nerves. The capsule of the tumor was opened, and 1.6 Gm. of solid yellow tumor tissue was removed. No cysts were encountered. There was no evidence of posterior extension of the tumor, which was a chromophobic adenoma.

A good recovery was made from the operative procedure, and on the twelfth postoperative day he was given a roentgenologic treatment (234 r). A severe reaction followed during the night. Eighteen hours later he was in deep coma. The blood sugar was 18 mg. per hundred cubic centimeters. Dextrose in sodium chloride solution was administered. For four days his condition was poor. He was given a continuous infusion of dextrose solution to maintain the blood level between 50 and 70 mg. per hundred cubic centimeters. The carbon dioxide-combining power and the chlorides, calcium, phosphorus and nonprotein nitrogen of the blood remained within normal limits. On the fifth day after the reaction a regimen of desoxycorticosterone acetate (percorten®), 5 mg., and sodium chloride 8 Gm. daily was begun. Within two days he began to improve and food was taken by mouth. A glucose tolerance test three weeks after operation and a similar test two weeks later gave normal results. The basal metabolic rate six weeks after operation was —5 per cent. Approximately one month after the onset of his metabolic crisis he maintained a normal blood sugar on a normal diet.

The ophthalmoplegia commenced to disappear on the fifth postoperative day, when he was able to abduct the right eye slightly; and within a day or two the left eye could also be abducted. Reaction to light appeared in the right pupil at this time. Three weeks after operation he could elevate the right upper eyelid, and both eyes could be abducted fully. At this time the right fourth nerve

began to function and both pupils reacted to light. Two months after operation both eyes could be opened widely and both pupils responded to light, but there was still some divergence. He was discharged from the hospital on December 2, two months after operation. Four months after operation the ophthalmoplegia had disappeared completely and there was absence of diplopia. The visual fields appeared full on the confrontation test, and the visual acuity was 20/30 for each eye. Eight months after operation the visual fields were normal, and visual acuity was 20/15 and 20/20 in the right and the left eye, respectively.

*Comment.*—The occurrence of bilateral total ophthalmoplegia after an episode of excruciating pain in the head and face of a patient with acromegaly who has an enlarged sella turcica suggests sudden swelling of a pituitary tumor. Such swelling usually is attributable to bleeding within the adenoma. A principal point of interest in this case was the absence of demonstrable involvement of the fifth nerve and retention of normal corneal sensitivity; this observation seems of particular importance and is further commented on subsequently. Proof that the inciting development was sudden pressure is obvious because of the complete recovery of vision and visual fields and the complete disappearance of ophthalmoplegia without evidence of the "regeneration" phenomenon in either third nerve.

It is likely that before the episode which brought him for examination this patient exhibited only acromegaly as a sign of his pituitary tumor. Probably, as a result of hemorrhage, which may have been slight, there was rapid swelling of the gland with pressure on the cavernous sinuses and on the overlying optic chiasm. Operation for removal of the tumor had the same effect as the opening of a cyst which was under pressure.

CASE 2.—A white man aged 52 considered himself perfectly well until he experienced a sudden excruciating pain in the head and face. Within forty-eight hours he exhibited total ophthalmoplegia bilaterally and had lost all vision, including the ability to perceive light. There was absence of demonstrable involvement of the fifth nerve on either side. Roentgenograms of the skull showed an enlarged sella turcica with erosion of the base. An adenoma of the pituitary gland was removed surgically. The extraocular muscles rapidly developed normal power. The patient remained permanently blind.

On Dec. 7, 1948 the patient awakened with pain in both temples and about the right eye. He complained of discomfort in his chest. During the evening there was vomiting and he became restless. On the following morning, December 8, he had pronounced photophobia and vision in the right eye was blurred. There was some drooping of the right upper eyelid. He became delirious, and late in the day he stated that he was blind. He was admitted to the University Hospital on December 9.

On admission he was totally blind and was delirious. The neck was stiff, and there was total bilateral ophthalmoplegia. The temperature was 105 F. He was completely disoriented as to time and place but responded promptly to painful stimuli. There was no weakness, atrophy, tremor or muscular fibrillation. All sensations were intact, including the responses to corneal stimulation. The tendon reflexes were equal and active. The abdominal reflexes were absent.

Blood studies showed leukocytosis (white cell count 18,700). Lumbar puncture produced fluid which contained 1,017 white cells per cubic millimeter and 122 mg. of protein and 76 mg. of sugar per hundred cubic centimeters and gave a 3 plus reaction for globulin. Smears and culture of the spinal fluid revealed no pathogens; blood cultures were sterile. Subsequent studies of the spinal fluid showed a gradual approach to normal.

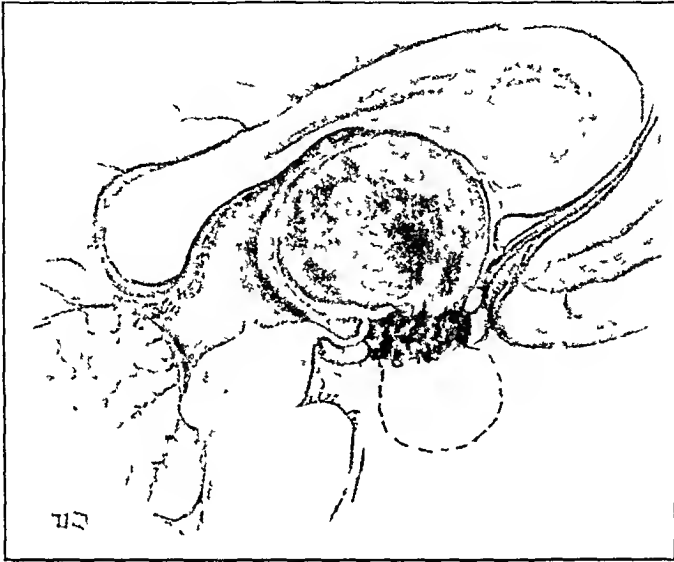


Fig. 1—Hypothalamic extension of an adenoma, filled with blood. From Jefferson.<sup>2</sup>

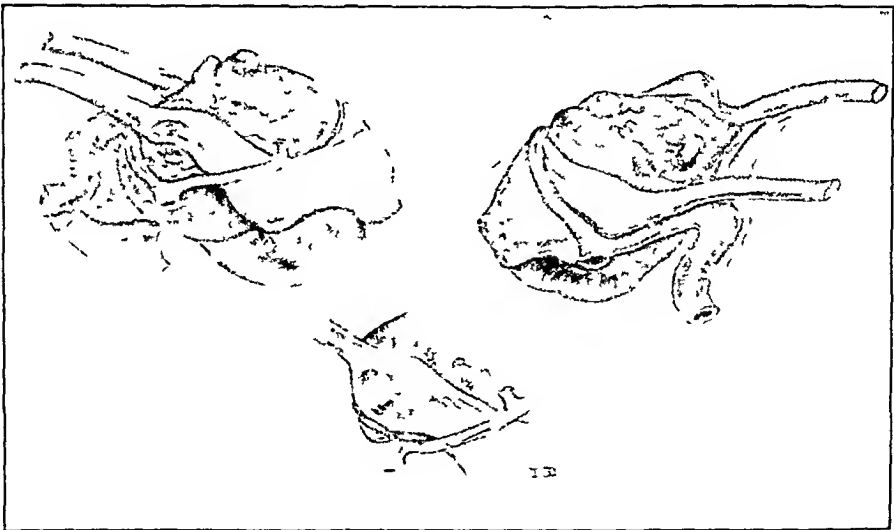


Fig. 2.—Chromophobic adenoma, with herniation of the adenoma compressing the outer fibers of the optic nerve (left eye blind). There is compression of the dorsum of the chiasma by anterior cerebral arteries. From Jefferson.<sup>2</sup>

Roentgenograms of the skull revealed an enlarged sella turcica, with erosion of the floor and posterior clinoid processes and sharpening of the anterior clinoid processes.

Permission for intracranial exploration was at first refused; but on December 18, at which time the ophthalmoplegia was unchanged and the patient was completely blind, a right frontal craniotomy was performed. A large adenoma of the pituitary gland was removed. Recovery from operation was uninterrupted.

On his discharge, on December 28, there had been recovery of function of the left sixth nerve and partial return of function of the right third nerve. On Feb. 15, 1949 at Dr. Arnold's office, the extraocular movements were fairly normal,

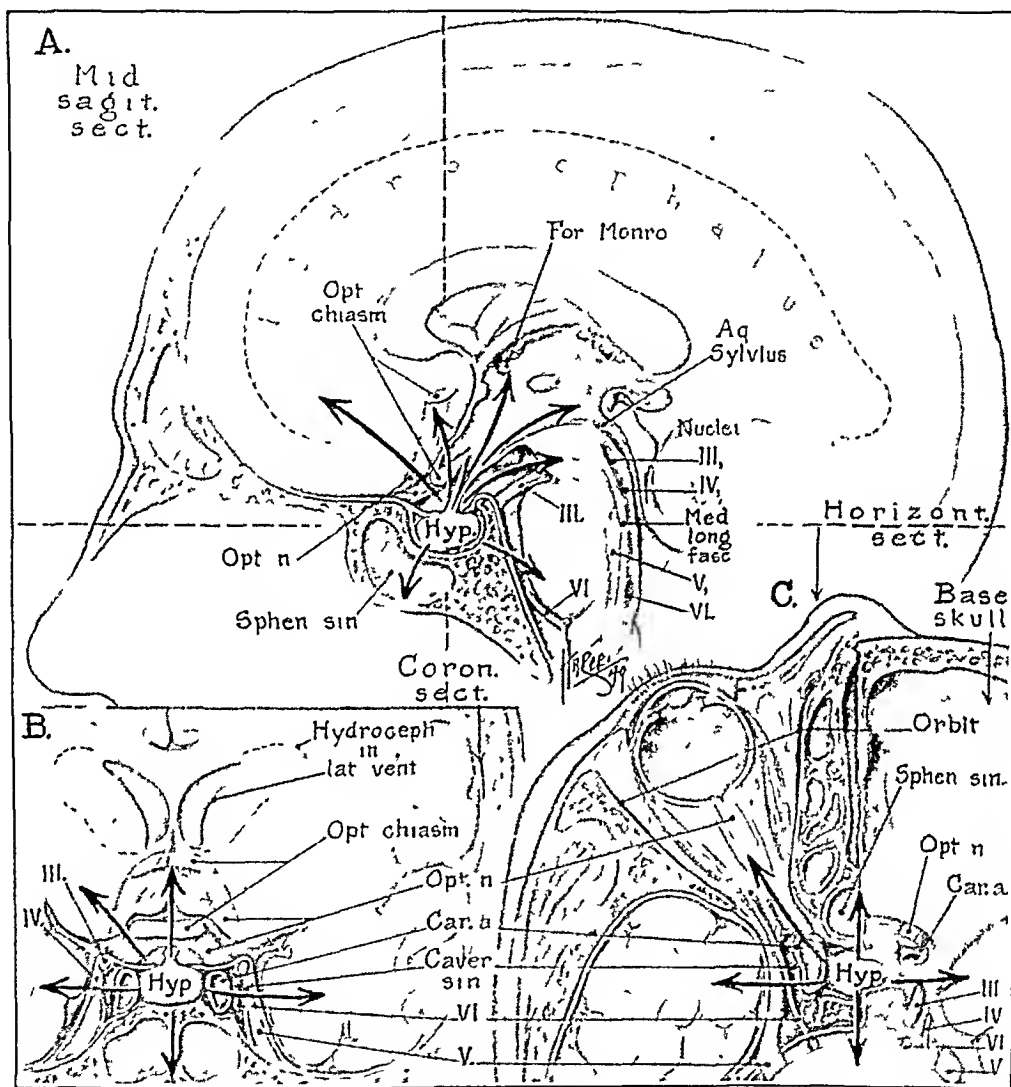


Fig. 3.—Diagram illustrating routes of extension of adenomas of the pituitary gland. Intracellar adenomas may extend through a solid layer of bone into the sphenoid sinus (*A*). Oftener, extension is upward through the diaphragma sellae, when the optic chiasm is usually affected (*A*). There may be progress forward, with involvement of the frontal lobe. The third ventricle may be filled with tumor and the foramen of Monro obstructed on one or both sides, or the aqueduct of Sylvius may be obstructed. Extension along the base may develop, as shown in *A*. Lateral spread involving the cavernous sinuses is shown in *B*. It will be noted that there is no bony wall lateral to the hypophysis (*B*; *A*). Obstruction to the cavernous sinuses may account for proptosis (*C*). Lateral spread accounts for involvement of the temporal lobe (*C*).

and there was movement of the pupils on attempted convergence, but the patient was quite blind.

*Comment.*—It is apparent that the condition in this case, except for the sudden and permanent blindness, was identical with that in case 1. Again, there was no demonstrable involvement of the fifth nerve.

The sudden loss of vision is interesting. Two figures taken from Jefferson's<sup>2</sup> paper explain the occurrence (figs. 1 and 2). They are included without further comment.

#### ROUTES OF EXTENSION OF PITUITARY ADENOMAS

Figure 3 indicates the possible extensions of pituitary adenomas. It is hoped that it may be useful in visualizing the development of signs which occasionally are associated with tumors of the pituitary gland and which cause confusion in diagnosis, namely, proptosis, hydrocephalus, ophthalmoplegia and involvements of the frontal and temporal lobes, as well as of the brain stem and cerebellum.

#### THE CAVERNOUS SINUS AND ITS NERVES

Figure 4 is a drawing of the cavernous sinus which has been designed to allow visualization of the arrangement of the nerves within the sinus at various levels.

#### RETENTION OF FUNCTION OF THE FIFTH NERVE AND THE CORNEAL REFLEX

Particular mention has been made of the absence of demonstrable involvement of the fifth nerve in the 2 cases of ophthalmoplegia associated with pituitary tumor. If pressure on the cavernous sinuses is the proper explanation of ophthalmoplegia in these cases, and it would seem to be the only reasonable explanation on the basis both of the anatomy of the parts and of the complete recovery, it is difficult to understand why the first and second division of the fifth nerve were not affected. Certainly, these sensory branches of the fifth nerve are as available for pressure as are the other (motor) nerves. With respect to this retention of function of the fifth nerve, it is obvious that the pains in the head and face are due to irritation of branches of the sensory elements of this nerve. Experimental work by Denny-Brown<sup>4</sup> seems to establish a factual explanation. He found that with carefully controlled cuff pressure he could abolish the function of motor nerves before that of sensory nerves. Undoubtedly, this observation applies to the nerves within the cavernous sinus; sensory nerves continue to function, since they are more resistant to pressure than motor nerves, and thus ophthalmoplegia may be complete before there is demonstrable sensory loss. The sequence of events from pressure is probably (1) paresthesias, (2) motor loss and (3) sensory loss. Thus, pressure on the cavernous sinuses

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4. Denny-Brown, D., and Brenner, C.: Paralysis of Nerve Induced by Direct Pressure and by Tourniquet, *Arch. Neurol. & Psychiat.* 51:1-26 (July) 1944.

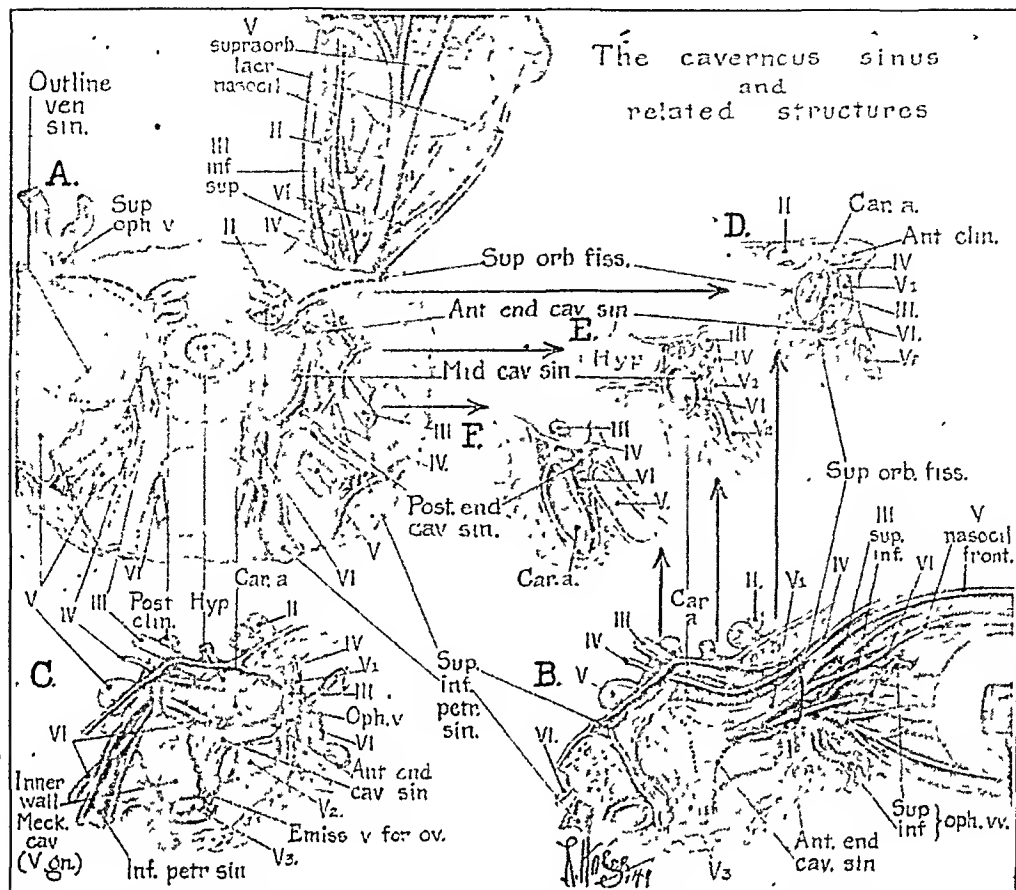


Fig. 4.—The cavernous sinus. (A) Top view. The dotted lines indicate the position of the sinuses. The right side is dissected. (B) Right lateral view. The wall of the sinus is dissected away, and the position of the nerves is shown. (C) Deeper dissection than that shown in B. The tip of the petrous bone is removed. (D; E; F) Vertical sections through the posterior, middle and anterior parts of the cavernous sinus, respectively.

A wide variation exists in the size and arrangement of the sinuses and the ophthalmic veins in normal persons. The superior petrosal sinus is inconstant. The intercavernous sinuses are variable in size. The transverse (basilar) sinus, which connects the inferior petrosal sinuses, is shown in A but is not identified in the drawing. It is always a large sinus.

**Nerves in the Cavernous Sinus:** The sixth nerve is shown at the base of the skull in A. It passes within the inferior petrosal sinus under the petrosphenoid ligament to enter the body of the sinus, where it lies lateral and inferior to the carotid artery. In C it can be seen that the sixth nerve enters the sinus before the third and fourth nerves. In the posterior part of the cavernous sinus only the sixth nerve and the first and second divisions of the fifth nerve are present. Farther forward in the sinus the sixth nerve becomes lateral and inferior (E; D). It enters the superior orbital (sphenoid) fissure inferiorly and laterally (B; A).

The third nerve enters the cavernous sinus at the junction of the posterior and the middle third (F; E). Its position anteriorly and directly lateral to the carotid artery is seen (E; D). It passes through the superior orbital fissure medial to and above the sixth nerve (C; B). This nerve divides into its superior and inferior branches within the cavernous sinus (Gifford, H., Jr.: ARCH. OPHTH. 41:5 [Jan.] 1949); unfortunately, this is not shown in the drawing.

The fourth nerve enters the sinus just posterior to and below the entrance of the third nerve. Its course through the sinus is shown in A. Its position in the lateral wall of the sinus is seen in A and D. It goes through the upper part of the superior orbital fissure after passing medial to the third nerve (B).

The gasserian ganglion is seen to lie in Meckel's cavity (C; B). The sensory root and the three divisions are seen in B. The ophthalmic and maxillary nerves are seen to lie in the posterior part of the sinus (B; F). The position of the nerve in the lateral wall of the sinus is seen in E and D. The branches of the ophthalmic division are shown in A and B.

produces (1) pain in the distribution of the sensory nerves, (2) motor loss and (3) sensory loss, which in the cases here described did not develop.

If ophthalmoplegia in these cases has been properly explained as evidences of pressure within the cavernous sinus, it follows that a similar retention of sensory function and of the corneal reflex may be anticipated with anteriorly situated aneurysms and with some aneurysms within the cavernous sinus itself. The retention of the corneal reflex has been observed in many of our cases of anteriorly situated aneurysms.

When corneal anesthesia is under consideration as an evidence of involvement of the fifth nerve, it seems advisable to mention its occurrence with tumor of the cerebellopontile angle, when it is a classic sign. Corneal anesthesia is characteristically present when other evidences of involvement of the fifth nerve are not demonstrable and there is an incomplete facial nerve palsy. It is generally believed that the association of incomplete palsies of the fifth and seventh nerves accounts for the loss of the reflex, since each of these nerves forms part of the reflex arc. Thus, early loss of the corneal reflex with tumors of the angle does not contradict what has been said concerning its persistence in the cases reported in this paper.

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## ACUTE TRACHOMA

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IN THOSE countries in which trachoma is epidemic and affects a high percentage of the population, infection almost always occurs in the preschool years, with an insidious onset and insignificant symptoms. Morax's early studies<sup>1</sup> in Egypt led him to believe that trachoma with acute symptoms was always complicated by secondary infection with one or more of the bacteria which are responsible for the acute ophthalmias, e. g., the Koch-Weeks bacillus or the gonococcus. The extraordinary prevalence and seriousness of the acute ophthalmias in Egypt have been the subject of numerous reports, and the term "ophthalmia aegyptiaca"<sup>2</sup> has been used to designate the acute manifestations of a conjunctivitis which is a mixture of two or of all three of the commonest infections, i. e., trachoma, gonococcic conjunctivitis and acute infectious conjunctivitis (Koch-Weeks conjunctivitis).

In those areas, however, in which trachoma is endemic only, as it is in the United States as a whole, the disease has frequently appeared to be free from secondary bacterial infection and to be acute at onset, particularly when contracted in adult life. Among the Indians of the American Southwest, on the other hand, where conditions are more like those in Egypt, the onset of the disease, which usually occurs in early childhood, seems to be almost always insidious.

The present study is an analysis of 14 cases of acute trachoma which I have observed during the course of intensive studies on the etiology and treatment of the disease in Egypt, Tunisia, Iowa, New York, Arizona, New Mexico, Florida and California.

The various criteria on which a diagnosis of trachoma may be based have been defined by many authors. In this study diagnosis depended on the gross or biomicroscopic demonstration of pannus in conjunction with at least one of the following findings: (1) follicles of the upper

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1. Morax, V.: *Recherches clinique et bacteriologiques sur la conjonctivite granuleuse d'Egypte*, Paris, J. Therenot, 1902.

2. Wilson, R. P.: *Ophthalmia Aegyptiaca*, *Am. J. Ophth.* **15**:397 (May) 1932.



tarsus; (2) limbal follicles or their cicatricial remains, known as Herbert's peripheral pits; (3) scarring of the upper tarsus, and (4) Halberstaedter-Prowazek inclusion bodies.

#### ACUTE EXACERBATIONS OF PREEXISTING CHRONIC TRACHOMA

Six cases in the series fell in this category (table 1). In 3 of them (cases 1, 2 and 5) repeated cultures revealed no evidence of secondary bacterial infection, and in 3 (cases 3, 4 and 6) there was secondary infection, with hemoglobinophilic bacteria (Koch-Weeks bacilli) in 1, with *Staphylococcus aureus* in another, and with *Diplococcus pneu-*

TABLE 1.—*Observations on 6 Patients with Chronic Trachoma with Acute Exacerbations*

Case No.	Age	Sex	Smears	Scrapings	Cultures	Preauricular Nodes	Conjunctiva	Cornea	Results of Treatment
1	55	M	Polymorphonuclear cells; no bacteria	Loaded with inclusions	Normal flora	Palpable	Papillary hypertrophy predominant	Severe epithelial keratitis	Slow improvement with copper sulfate
2	26	M	Polymorphonuclear cells; no bacteria	Many inclusions	Normal flora	Palpable	Papillary hypertrophy predominant	Severe epithelial keratitis	Rapid healing with sulfanilamide
3	10	M	Polymorphonuclear cells; pneumococci	Few inclusions	<i>D. pneumoniae</i>	Not palpable	Papillary hypertrophy predominant	Minimal epithelial keratitis	Healing after 20 days with sulfadiazine therapy
4	42	F	Polymorphonuclear cells; many staphylococci	Few inclusions; many cocci	<i>Staph. aureus</i>	Not palpable	Papillary hypertrophy predominant	Epithelial keratitis, severest below	Healing after 21 days with sulfadiazine therapy
5	22	M	Polymorphonuclear cells; no bacteria	Many inclusions	Normal flora	Not palpable	Papillary hypertrophy predominant	Severe epithelial keratitis	Rapid response to sulfadiazine therapy
6	26	M	Polymorphonuclear cells; Koch-Weeks bacilli	No inclusions seen	Hemoglobinophilic bacteria (Koch-Weeks)	Not palpable	Papillary hypertrophy predominant	Minimal epithelial keratitis	Healing after 26 days with sulfadiazine therapy

moniae in the third. The first case, observed in Iowa in 1934, was of unusual interest and may be described briefly as follows:

CASE A 1.—G. Y., a Fox Indian aged 55, had a history of trachoma of fifty years' duration. He was hospitalized with bilateral purulent conjunctivitis of extreme severity. Repeated smears showed no bacteria, and numerous cultures failed to reveal pathogenic bacteria. Epithelial scrapings, however, showed extraordinary numbers of trachoma inclusions, as many as 200 appearing in a single slide. In addition, there were masses of readily identifiable free elementary bodies, a most unusual finding in trachoma. The acute attack subsided gradually under copper sulfate therapy, leaving the previously scarred conjunctivas and corneas virtually unchanged.

This case was certainly an instance of an acute exacerbation due entirely to the virus of trachoma. In cases 2 and 5 the conditions were similar but less severe; the acute attack in each subsided rapidly on sulfonamide therapy.

Of the 3 cases in this group with secondary bacterial infection, case 6 may be considered typical.

CASE 6.—P. M., aged 26, a salesman, had acute conjunctivitis of the right eye with considerable mucopurulent exudate. There was no palpable preauricular node. In the papillary hypertrophy of the tarsal conjunctiva, which was most pronounced on the upper tarsus, buried follicles could be made out. There was a typical trachomatous pannus with scattered infiltrates and punctate epithelial lesions of the upper portion of the cornea, which were visible when stained with fluorescein. On questioning, the patient gave a history of chronic irritation of both eyes of many years' duration and stated that his mother had had irritated eyes with poor vision and ingrowing lashes.

Smears of the exudate showed polymorphonuclear leukocytes predominating, with many small, slender gram-negative rods having the morphologic appearance of the Koch-Weeks bacillus, occurring both intracellularly and free. Epithelial scrapings showed many epithelial cells with bacilli on their surfaces. No inclusion bodies were demonstrated. Cultures revealed typical hemoglobinophilic bacteria.

Oral sulfadiazine therapy was instituted, and the acute symptoms subsided rapidly. In the course of a twenty-six day period of treatment, the papillary hypertrophy disappeared; the cornea became free from subepithelial infiltrates, and the conjunctival cicatrization of stage III trachoma (MacCallan's classification<sup>3</sup>), previously obscured by the papillary hypertrophy, became visible. The left eye, which displayed mild stage III trachoma with pannus, healed under the sulfonamide therapy. Healing was slow, however, and there were still follicles when the sulfadiazine therapy was discontinued. These gradually absorbed over a period of weeks, until the conjunctiva had become smooth.

This case was clearly one of trachoma with acute symptoms due to secondary infection with the Koch-Weeks bacillus.

#### TRACHOMA OF ACUTE ONSET

Eight cases of trachoma which was acute at onset were observed in the course of this study. In 2 the disease was the result of experimental inoculations, and in 6 cases the infection occurred spontaneously. One of the 2 experimental inoculations and 1 of the 6 spontaneous infections were complicated by secondary infection with bacteria.

*Experimental Inoculations* (table 2).—The 2 cases in this category have already been reported.<sup>4</sup>

CASE 7.—The first experimental inoculation was in a young male volunteer with an incurable and eventually fatal renal disease. Epithelial scrapings from a patient with stage IIa (follicular) trachoma were brushed onto the upper and lower tarsal conjunctivas of one eye with a cotton swab. Seven days later trachoma of acute onset developed. The disease was frankly purulent. Smears showed hemoglobinophilic bacteria (Koch-Weeks bacilli), and epithelial scrapings showed typical trachoma inclusion bodies. The acute symptoms lasted about two

3. MacCallan, A. F.: *Trachoma and Its Complications in Egypt*, London, Cambridge University Press, 1913.

4. Thygeson, P.; Proctor, F. I., and Richards, P.: Etiologic Significance of the Elementary Body in Trachoma, *Am. J. Ophth.* 18:811 (Sept.) 1935.

weeks, when typical trachoma stage IIa with early (biomicroscopic) pannus developed. This was evidently a trachoma with secondary infection from onset, and it was not possible to say whether the acute symptoms were due to the bacterial infection or to the trachoma itself.

CASE 8.—The second experimental inoculation was in a male volunteer aged 50 who had incurable carcinoma. He was similarly inoculated with a bacteria-free filtrate of pooled epithelial scrapings from patients with active trachoma. Exactly five days afterward a violently acute conjunctivitis with chemosis of the bulbar conjunctiva developed. Smears and cultures revealed no bacteria, but epithelial scrapings were loaded with inclusion bodies. The symptoms remained acute for about three weeks, when the intensity of the inflammation began gradually to subside. The first extension of limbal vessels occurred on the sixth day, and typical trachoma pannus had developed by the sixth week. The disease remained active for about a year despite intensive treatment with copper sulfate but had healed entirely at the time of the patient's death, fifteen months after inoculation. The healed conjunctiva showed extensive scarring. Secondary bacterial infection never occurred.

TABLE 2.—*Observations on Experimental Trachoma Induced in Human Volunteers*

Case No.	Age	Sex	Smears	Scrapings	Cultures	Preauricular Nodes	Conjunctiva	Cornea	Results of Treatment
7	22	M	Polymorphonuclear cells; many slender rods, like Koch-Weeks bacilli	Few inclusions Koch-Weeks bacilli	Not made	Not palpable	Papillary hypertrophy predominant	Early onset of pannus	Slow response to silver nitrate and copper sulfate therapy
8	50	M	Polymorphonuclear cells; no bacteria	Many inclusions	Normal flora	Palpable	Papillary hypertrophy predominant; chemosis of bulbar conjunctiva	Extremely severe epithelial keratitis; early onset of pannus	Slow response to copper sulfate therapy; healing in 1 yr.

*Spontaneous Infections* (table 3).—Of the 6 cases of spontaneous trachoma observed at onset or shortly thereafter, 3 occurred in New York, 2 in California and 1 in Arizona. Five were of white persons, and 1 was of an Apache Indian.

CASE 9.—M. G., aged 52, a New York business man, had onset of acute conjunctivitis of the right eye after a business trip west. The conjunctivitis was papillary in type and was characterized by a dense cellular infiltration of the conjunctiva, particularly intense in the conjunctiva of the upper tarsus and fornix. An intense, fluorescein-staining epithelial keratitis involved the entire surface of the cornea, but was more pronounced over the upper third. The conjunctiva of the upper limbus was edematous and infiltrated, and discharge was abundant and mucopurulent. The preauricular node was palpable but not tender. On the fourth day of the illness, minute subepithelial infiltrates were seen scattered over the upper third of the cornea but were densest close to the limbal vessels. The limbal vessels were engorged, but extension in the form of pannus was not observed until the eleventh day. The pannus developed rapidly, so that by the twentieth day examination with the slit lamp showed a typical trachomatous pannus with extension of limbal loops into the cornea around the entire circumference, but more marked above.

Cultures and smears in this case were made daily during the first weeks of the illness, but no pathogenic bacteria were found. Epithelial scrapings showed many Halberstaedter-Prowazek inclusions. These were more than twice as numerous in scrapings from the upper tarsus as they were from the lower tarsus. The exudate was always characterized by a predominance of polymorphonuclear leukocytes.

The diagnosis of trachoma in this case was based on the findings of the inclusion bodies in conjunction with corneal changes. The only disease considered in the differential diagnosis was inclusion conjunctivitis, and this could be ruled out by the presence of the keratitis and pannus.

Treatment with sulfanilamide over a period of three weeks led to healing. On examination with the slit lamp, the healed tarsal conjunctiva showed a few

TABLE 3.—*Observations on 6 Patients With Trachoma of Acute Onset*

Case No.	Age	Sex	Smears	Scrapings	Cultures	Preauricular Nodes	Conjunctiva	Cornea	Results of Treatment
9	52	M	Polymorphonuclear cells; no bacteria	Many inclusions	Normal flora	Palpable	Papillary hypertrophy predominant	Severe epithelial keratitis	Rapid response to sulfanilamide
10	38	M	Polymorphonuclear cells; no bacteria	Many inclusions	Normal flora	Palpable	Papillary hypertrophy predominant	Severe epithelial keratitis; incipient pannus	Rapid response to sulfanilamide
11	28	M	Polymorphonuclear cells; no bacteria	Many inclusions	Normal flora	Not palpable	Papillary hypertrophy predominant	Severe epithelial keratitis; incipient pannus	Rapid response to sulfanilamide
12	23	M	Polymorphonuclear cells; no bacteria	Many inclusions	Normal flora	Not palpable	Papillary hypertrophy predominant	Severe epithelial keratitis; incipient pannus	Rapid response to sulfanilamide
13	23	M	Polymorphonuclear cells; no bacteria	Many inclusions	Normal flora	Not palpable	Papillary hypertrophy predominant	Severe epithelial keratitis; incipient pannus	Rapid response to sulfanilamide
14	26	F	Polymorphonuclear cells; Koch-Weeks bacilli	Few inclusions	Hemo-globinophilic bacteria (Koch-Weeks)	Palpable	Papillary hypertrophy predominant	Mild epithelial keratitis; incipient pannus	Satisfactory response to sulfanilamide

minute scars, the cornea became free from infiltrates but the pannus vessels persisted. This case was clearly one of pure acute trachoma uncomplicated by secondary infection.

CASE 10.—G. F., aged 38, a mechanic, had bilateral conjunctivitis. The onset was acute and characterized by intense papillary hypertrophy of the conjunctiva, especially over the upper tarsus, and by mucopurulent exudation and palpable, but not tender, preauricular nodes. As in case 9, there was from onset a severe epithelial keratitis with subsequent development of subepithelial infiltrates and extension of limbal vessels. A characteristic feature of the disease was the infiltration and edema of the region of the upper limbus. This formed a sort of roll, the curve of which was easily recognizable, both grossly and with the slit lamp.

Repeated smears and cultures revealed no pathogenic bacteria, but cytoplasmic inclusions were abundant. On one slide as many as 20 per cent of the cells had

inclusions, a startling difference from the findings in any typical case of trachoma in the chronic stage.

The conjunctivitis continued in its acute phase for three weeks. Treatment with sulfanilamide was then instituted, and in three weeks the condition was healed. As the extreme papillary hypertrophy disappeared in the course of healing, follicles which had been masked by the cellular infiltration were exposed to view. After healing there was a minimal amount of conjunctival cicatrization and persistence of pannus vessels. This was evidently a case of pure trachoma of acute onset, uncomplicated by secondary infection.

CASE 11.—S. F., aged 28, a salesman, had bilateral acute conjunctivitis with edema of the bulbar conjunctiva and abundant mucopurulent exudate. When seen on the third day of symptoms, the conjunctivas exhibited the heavy infiltrate and papillary hypertrophy typical of stage IIb trachoma. The preauricular nodes, unlike those in cases 9 and 10, were not palpable, but the corneas showed the same severe punctate epithelial staining. Subepithelial infiltrates were first seen on the fifth day of the illness, and extension of limbal vessels into the corneas, on the tenth day. By the eighteenth day a typical incipient pannus was demonstrable. Sulfanilamide therapy was begun on this day and was continued over a four week period. The response was rapid, and healing was obtained without difficulty.

CASE 12.—A. D., aged 23, a truck driver, had onset of unilateral acute conjunctivitis. The conjunctivitis was severe, but there was no swelling of the preauricular node and the edema of the bulbar conjunctiva was limited to the region of the upper limbus. There was an unusually severe punctate epithelial keratitis with numerous subepithelial infiltrates, particularly in the pupillary area. The effect on vision was striking, the visual acuity having been reduced to 20/200 before therapy was started, on the twentieth day. Typical incipient pannus was demonstrated on the fifteenth day. A three week course of sulfadiazine led to healing and return of vision to 20/20, but nebulous scars persisted in the cornea. Smears and cultures revealed no secondary bacterial infection, but inclusion bodies were demonstrated without difficulty in epithelial scrapings until therapy was instituted. This case could be described as one of pure acute trachoma with unusual corneal manifestations.

CASE 13.—D. J., aged 23, an air corps officer in active service, had onset of acute conjunctivitis of the right eye two months after returning from India. The conjunctivitis was papillary in type and displayed the thickening of the tarsal conjunctiva and the folds in the fornices which are so characteristic of viral conjunctivitis, as opposed to bacterial conjunctivitis. When the eye was first seen on the tenth day of the illness, there was already extension of limbal capillary loops into the cornea, and three days later the picture of incipient trachoma pannus was complete. No preauricular adenopathy was noted. Epithelial keratitis was severe, and subepithelial infiltrates were prominent. Sulfadiazine, begun on the twentieth day of the disease, led to rapid subsidence of the acute symptoms and to healing after a three week course. There was no evidence of secondary bacterial infection, but numerous epithelial cell inclusions were readily demonstrable. The case was clearly one of pure trachoma with acute onset.

CASE 14.—F. M., aged 26, a nurse, had onset of bilateral acute conjunctivitis with slight preauricular adenopathy. There was an abundant purulent exudate, which on smear and culture revealed many Koch-Weeks bacilli. The conjunctivitis was treated daily during the first ten days with applications of silver nitrate and use of 5 per cent sulfathiazole ointment locally. When the conjunctivitis failed

to improve with this treatment, the case was restudied and evidence of an underlying trachoma deduced from the presence of typical inclusion bodies in epithelial scrapings and from corneal changes involving the region of the upper limbus. The inclusion bodies were relatively few, and the corneal changes were mild in comparison with those in the other cases in this series. Sulfadiazine therapy was instituted and improvement was noted on the third day. Healing was complete in one month. This case was evidently one of acute trachoma in which a bacterial infection contributed to the acute symptoms.

#### DIFFERENTIAL DIAGNOSIS OF ACUTE TRACHOMA

When the acute symptoms of acute trachoma are due to an exacerbation of previously existing trachoma, or to an acute bacterial infection engrafted on chronic trachoma, the diagnosis rests on the presence of the characteristic stigmas of trachoma, particularly cicatrization and pannus, and offers no serious difficulty. Trachoma which is acute at



Fig. 1.—Acute trachoma at onset, illustrating extreme papillary hypertrophy of the conjunctiva of the upper tarsus.

onset, on the other hand, is more difficult to diagnose and may be overlooked in this country because of its rarity.

The disease should be suspected in any case in which there are severe infiltration and papillary hypertrophy of the conjunctiva of the upper tarsus with obliteration of the conjunctival vessels and meibomian markings (fig. 1). Among the bacterial conjunctivitis, gonococcic conjunctivitis alone displays a comparably severe cellular infiltration, and in this disease the abundance of the purulent exudate is a differentiating feature. In acute trachoma the exudate is typically mucopurulent, but in the present series it was abundant only in the 2 cases complicated by infection with the Koch-Weeks bacillus (acute infectious conjunctivitis).

Differentiation from inclusion conjunctivitis appeared to offer the only serious diagnostic problem. In my experience, however, inclusion conjunctivitis, even in the acute papillary form, has not been complicated

by corneal changes, whereas in trachoma of acute onset the corneal changes have occurred simultaneously with the conjunctival changes. In this series the changes in the upper limbus, consisting in edema and infiltration of the conjunctiva at the limbus and in early extension of the limbal capillaries to form incipient trachoma pannus, were of particular diagnostic value.

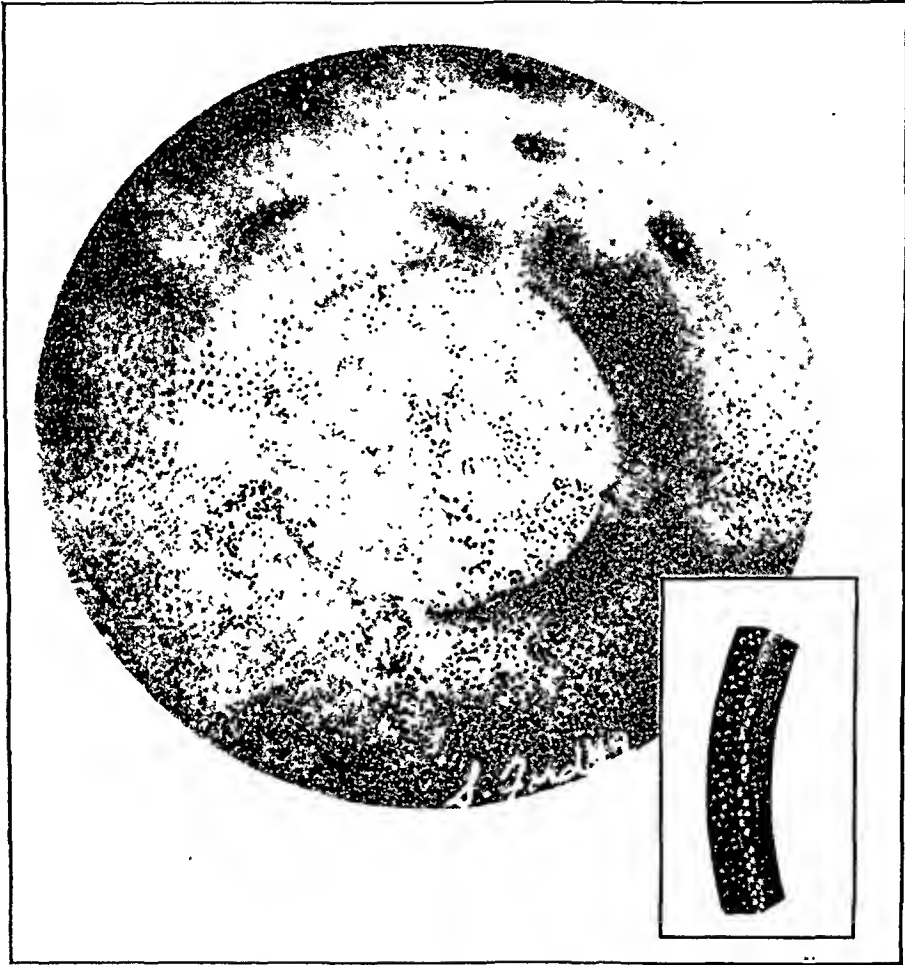


Fig. 2.—Drawing of the cornea in a case of acute trachoma at onset, illustrating the punctate epithelial changes and the subepithelial infiltration so characteristic of the disease. This case was unusual with respect to the distribution of the epithelial changes, which are usually much more pronounced adjacent to the upper limbus.

Among other types of acute keratoconjunctivitis, only acute staphylococcal keratoconjunctivitis and epidemic keratoconjunctivitis would seem to need consideration in the differential diagnosis of acute trachoma. A pannus somewhat resembling trachoma pannus can sometimes develop in cases of recurrent staphylococcal infection when catarrhal infiltrates have occurred repeatedly at the upper limbus. This

is confusing, but in a staphylococcic infection there are no conjunctival scars and no inclusion bodies.

Epidemic keratoconjunctivitis would seem to be less of a problem, in view of the round corneal infiltrates which characterize it, but at least one set of investigators (Feigenbaum, Michaelson and Kornblüth<sup>5</sup>) have considered differentiation from this condition diagnostically important. In my experience, in only 1 case of acute trachoma was the condition clinically suggestive of epidemic keratoconjunctivitis. In this case (table 3, case 12) there were large round infiltrates in the pupillary area, but the presence of inclusion bodies and the cytologic character of the conjunctival exudate (polymorphonuclear cells predominating), as well as the rapid response of the disease to sulfonamide therapy, established the diagnosis. It is well to mention in this connection, however, that in epidemic keratoconjunctivitis with pseudomembrane formation the exudate, which is loaded characteristically with mononuclear cells, may be more polymorphonuclear than mononuclear.

In the diagnosis of questionable cases the area of the upper limbus proved to be of great interest as the site of the following lesions: (1) edema and infiltration of the limbal conjunctiva, (2) punctate fluorescein-staining epithelial lesions (fig. 2), most marked in the upper third of the cornea near the limbus; (3) subepithelial infiltrates, most prominent in proximity to the limbal vessels, and (4) extension of the limbal vessels. The region of the limbus was also one of the best sites from which to take epithelial scrapings for the demonstration of inclusion bodies.

#### COMPARISON OF ACUTE AND CHRONIC TRACHOMA

Acute trachoma, whether pure or with secondary infection, was characterized in this series by the extreme papillary hypertrophy of trachoma IIb (MacCallan's classification). Moreover, the acute disease apparently developed from onset as stage IIb without first passing through stage I. Follicular formation seemed to occur simultaneously, however. This was evident from the fact that cells from the germinal center of the follicles (lymphoblasts) were frequently found in scrapings from the conjunctiva of the upper tarsus, and from the fact that follicles were unmasked as the papillary hypertrophy resolved under sulfonamide therapy. In the process of healing the follicles were inevitably the last lesions to disappear, as they are in chronic trachoma.

In acute trachoma the rapidity of the response to sulfonamide therapy is striking, and in sharp contrast to the slow response of chronic follicular (stage IIa) trachoma. In chronic trachoma there is

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5. Feigenbaum, A.; Michaelson, I. C., and Kornblüth, W.: Epidemic Kerato-Conjunctivitis in the Middle East, *Brit. J. Ophth.* 29:391 (Aug.) 1945.



almost never any improvement in the first week; in the cases of acute trachoma in this series improvement was usually evident in three or four days and measurable at the end of the first week.

The inclusion bodies of trachoma were always numerous in the pure acute disease and were always more numerous in scrapings from the conjunctiva of the upper tarsus than in scrapings from the conjunctiva of the lower tarsus. In this respect the acute disease differed sharply from the chronic disease, in which inclusion bodies are either few or not demonstrable. For this reason, a search for inclusion bodies has limited value in cases of chronic trachoma but has very great value in cases of acute trachoma.

One of the most striking aspects of acute trachoma in this series was the rapidity with which the limbal vessels invaded the cornea. In the second experimental inoculation, vessels had penetrated the cornea by the sixth day, and at the end of six weeks extensive pannus with a pannus ulcer had developed. In chronic trachoma many months would have been required for the formation of a pannus of this extent.

The low communicability of chronic trachoma is an established fact, but if the communicability of the disease is in direct relation to the number of viral bodies demonstrable in epithelial scrapings and to the amount of mucopurulent exudate, acute trachoma should be highly communicable; and there is some epidemiologic evidence to indicate that it is.

#### COMMENT

The observations in this small series of cases indicate that in the United States there is a certain limited incidence of acute trachoma in which the acute symptoms are due to the trachoma virus itself. Morax's conclusion that acute symptoms in trachoma always indicated secondary bacterial infection, however applicable in Egypt, certainly does not apply in the United States as a whole. It may have a limited application in the Indian country of the Southwest, where the disease is almost always acquired in infancy and is chronic from onset. Even in the Southwest, however, I observed several instances of acute exacerbations without secondary infection in the course of a five year study of the disease among the Apache Indians at Fort Apache, Ariz.

With 1 exception, the cases in this series were of adults. From my experience, it would seem that susceptibility to the trachoma virus increases with age. This would account for the fact that trachoma contracted in infancy usually has an insidious onset and trachoma contracted in adult life an acute onset. The amount of virus in the inoculum must also be a factor. This is suggested by the observation that almost all reported experimental human inoculations of trachoma have resulted in acute infections. Of the 2 experimental inoculations

included in this series, the second, in which the inoculum was a filtrate, resulted in trachoma with an extraordinarily severe onset, the symptoms of which included chemosis of the bulbar conjunctiva.

#### SUMMARY AND CONCLUSIONS

Fourteen cases of trachoma with acute symptoms are reported and analyzed. In 5 of the 14 cases there was secondary bacterial infection which could have accounted for the acute symptoms, but in the remaining 9 cases the trachoma was uncomplicated. The large number of viral inclusions and the occurrence of free viral elementary bodies in the exudate in these cases suggest that the acute symptoms were due to the action of the trachoma virus itself. It is concluded that trachoma, while ordinarily a chronic disease, sometimes has an acute phase.

Pure acute trachoma in this series was characterized by extreme papillary hypertrophy of the conjunctiva, by a mucopurulent exudate with polymorphonuclear leukocytes predominating, by an abundance of cytoplasmic inclusions in epithelial scrapings and by a severe and extensive punctate epithelial keratitis.

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## ENDOGENOUS INTRAOCULAR FUNGOUS INFECTION

### Report of a Case

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BOSTON

**E**NDOGENOUS fungous infections of the interior of the eyes are rare. Müller (1903)<sup>1</sup> described metastatic nodules in the retina from miliary actinomycosis arising in the lungs. Dimmer (1914)<sup>2</sup> reported choroidoscleritis due to a fungus thought to be *Aspergillus fumigatus*. Stock (1926)<sup>3</sup> reported abscesses of the vitreous and retina caused apparently by identical fungi. Verhoeff (1924)<sup>4</sup> reported a case of uveitis caused by an actinomycete-like organism in one eye of a patient after a postoperative infection by a fungus of a similar type in the fellow eye. Verhoeff (1926)<sup>5</sup> also reported idiopathic retino-choroiditis caused by a similar organism occurring in a patient after a febrile illness. Churchill and Stober (1914)<sup>6</sup> recovered blastomycetes from the vitreous of an eye of a patient with systemic blastomycosis, but no description of the ocular lesion was given. Schwartz (1931)<sup>7</sup> reported hypopyon iritis in one eye caused by a blastomycete occurring in a patient with blastomycetic abscesses elsewhere in the body. Cassady (1946)<sup>8</sup> reported severe nodular iritis due to a blastomycete occurring in a patient with generalized blastomycosis. Archangelsky (1928)<sup>9</sup>,

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From the Howe Laboratory of Ophthalmology, Harvard Medical School, and the Massachusetts Eye and Ear Infirmary.

1. Müller, L.: Ueber Veränderungen im Augenhintergrunde bei miliärer Aktinomykose, *Klin. Monatsbl. f. Augenh.* **41**(pt. 1): 236, 1903.

2. Dimmer, F.: Ein Fall von Schimmelpilzerkrankung des Auges, *Klin. Monatsbl. f. Augenh.* **51**(pt. 2): 194, 1913.

3. Stock, W.: Eine metastatische Ophthalmie durch Schimmelpilze, *Klin. Monatsbl. f. Augenh.* **76**(pt. 1): 49, 1926.

4. Verhoeff, F. H.: Mycosis of the Choroid Following Cataract Extraction, and Metastatic Choroiditis of the Other Eye, Producing the Clinical Picture of Sympathetic Uveitis, *Arch. Ophth.* **53**: 517 (Nov.) 1924.

5. Verhoeff, F. H.: A Case of Metastatic Intra-Ocular Mycosis, *Arch. Ophth.* **55**: 225 (May) 1926.

6. Churchill, T., and Stober, A. M.: A Case of Systemic Blastomycosis, *Arch. Int. Med.* **13**: 568 (April) 1914.

7. Schwartz, V. J.: Intra-Ocular Blastomycosis, *Arch. Ophth.* **5**: 581 (April) 1931.

8. Cassady, J. V.: Uveal Blastomycosis, *Arch. Ophth.* **35**: 84 (Feb.) 1946.

9. Archangelsky, W. N.: Ein Schimmelpilz unter der Netzhaut, der einen Zystizerkus simulierte, *Klin. Monatsbl. f. Augenh.* **81**(pt. 2): 211, 1928.

Rohner and Huber (1933)<sup>10</sup> and Lorenz (1933)<sup>11</sup> each reported a case of retinovitreal abscesses caused by an organism thought to be an aspergillus.<sup>12</sup> There have thus been previously reported a total of 11 cases of endogenous intraocular fungous infections, an actinomycete-like organism being causative in 3 cases, a blastomycete in 3 cases and an organism believed to be an aspergillus in 5 cases. In all but 1 case (that of Churchill and Stober) sections were examined histologically, but only in the cases of the blastomycotic infections were the lesions cultured.

The case to be reported here is also one of endogenous intraocular infection caused by an organism similar to that previously reported as an aspergillus. Like most of the other cases of aspergillar mycosis, the infection of the eye occurred in a patient who showed no evidence of fungous infection elsewhere in the body.

#### REPORT OF CASE<sup>13</sup>

*History.*—Z. L., a 70 year old Jewish housewife, had an uneventful medical history except for an episode several months before the ocular symptoms, when she had a cough and spat up blood-tinged sputum. The duration of this episode was only two or three days, and the incident was not considered of any importance by her physician.

The patient's ocular symptoms began with a sensation of "flies" before her left eye and, within a few hours, a sensation of a veil obscuring her vision. Whether or not the eye was red at the onset is uncertain; but when seen a few days later the eye was extremely red, and the lids of this eye were swollen. Pain was absent. There was no antecedent trauma, and, except for headaches which preceded the ocular symptoms, the patient had been in good health.

When she was seen by an ophthalmologist within two weeks after the onset, vision was nil; the conjunctiva was chemotic, and the eye was proptosed; the cornea was clear; the anterior chamber was shallow, and the ocular tension was normal. No red reflex was obtained from the fundus. The patient's temperature was not elevated, and the white blood cell count was normal. The clinical diagnosis was hemorrhage into the vitreous, but the complete loss of vision and the proptosis were unaccounted for.

The other eye was normal except for mild sclerosis of the retinal arteries.

One month after the onset severe pain developed in the eye. Examination at that time showed a steamy cornea, congested iris and extremely elevated

10. Rohner, M., and Huber, O.: Aspergillus als Ursache von Erblindung, Schweiz. med. Wchnschr. **1**: 181, 1933.

11. Lorenz, H.: Eine metastatische Ophthalmie durch Schimmelpilze, Dissertation, Munich, 1933.

12. Not included in the group is Fuchs's case of actinomycosis of the ciliary body (Ein Fall intraokulärer Aktinomykose, Arch. f. Ophth. **101**:24, 1920), since the condition is believed to have been a direct postoperative infection and, therefore, not of endogenous origin. Also not included is the report by Best (Demonstration beider durch Schimmelpilzinfektion erblindeter Augen einer Amsel, Deutsch. med. Wchnschr. **31**:1820, 1905) of an infection with *A. fumigatus* in the eyes of a bird because of the probable exogenous origin of the infection.

13. Dr. Frederick Salls and Dr. Benjamin Sachs furnished the clinical notes.

tension. The eye was removed. Noteworthy at the time of operation were extensive extraocular adhesions of the conjunctiva, sclera and Tenon's capsule.

The patient was last seen eight months after the enucleation. The socket appeared clean. The other eye appeared normal. The patient's general health remained good.

*Pathologic Examination.*—The globe was fixed in dilute solution of formaldehyde U. S. P. The globe when opened was noted to be of normal size and shape and contained a glistening white mass (presumably fat) on the episclera adjacent to the tendon of the inferior oblique muscle. When calottes were excised from

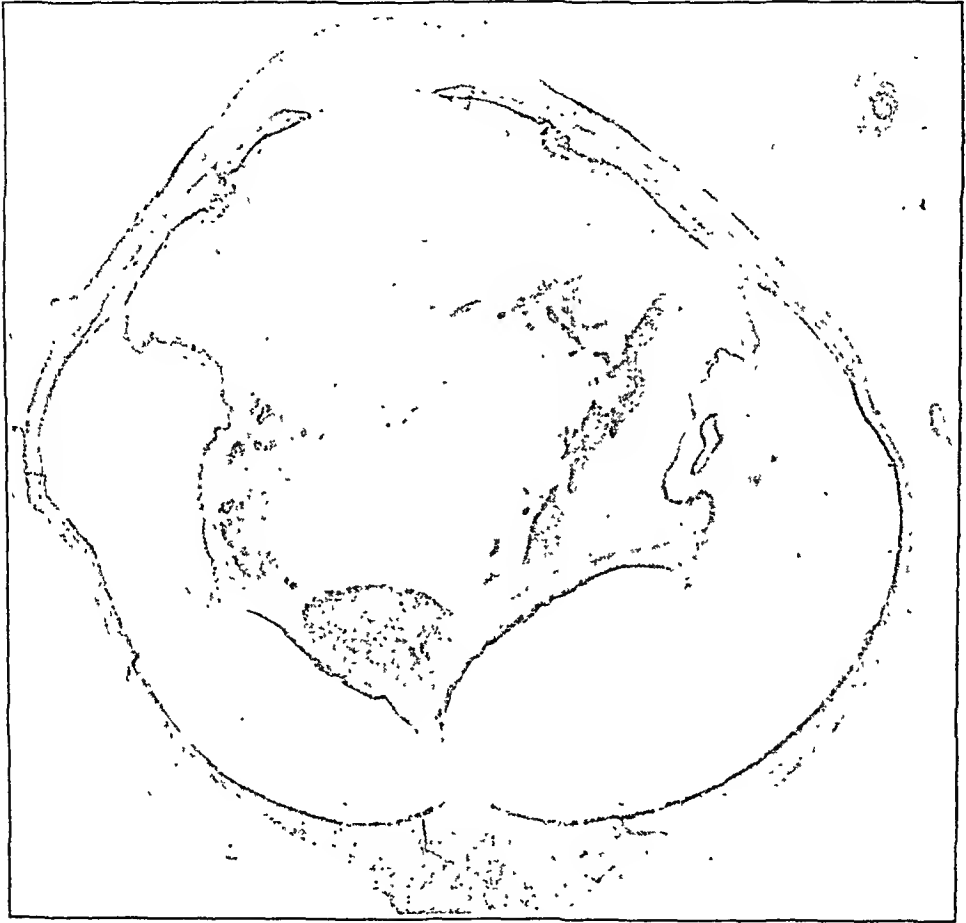


Fig. 1.—Cross section of the whole eye, showing almost complete separation of the retina with multiple abscesses on its inner surface and in the vitreous.

the upper and lower portions of the globe, the retina was seen to be partially separated and the posterior portion of the vitreous to contain a yellowish, granular material suggestive of abscess. The anterior portion of the vitreous was filled with a gelatinous material containing streaks continuous with the abscesses in the posterior part of the vitreous.

The globe was embedded in pyroxylin, and horizontal cross sections were made of the entire eye in routine fashion. Portions of the posterior half of the eye were subsequently re-embedded in paraffin. The sections were prepared variously with hematoxylin and eosin, the Gram stain, Verhoeff's modified

Gram stain, thionine, Giemsa's stain, Goodpasture's crystal violet and the Ziehl-Neelsen stain.

*Histologic Examination.*—The specimens consisted of cross sections of an eye showing in the gross an eosinophilic material in the aqueous, complete separation



Fig. 2.—Root of iris ( $\times 100$ ), showing an anterior synechia, exudate on the anterior surface of the iris and in the posterior chamber and cells (epithelioid) extending through the posterior surface of the iris.

of the retina and a multilobular basophilic material on the retina and in the vitreous (fig. 1). This material was most conspicuous in front of the disk.

The cornea was normal except for the presence of white blood cells (polymorphonuclear and round cells) and macrophages adherent to its endothelial

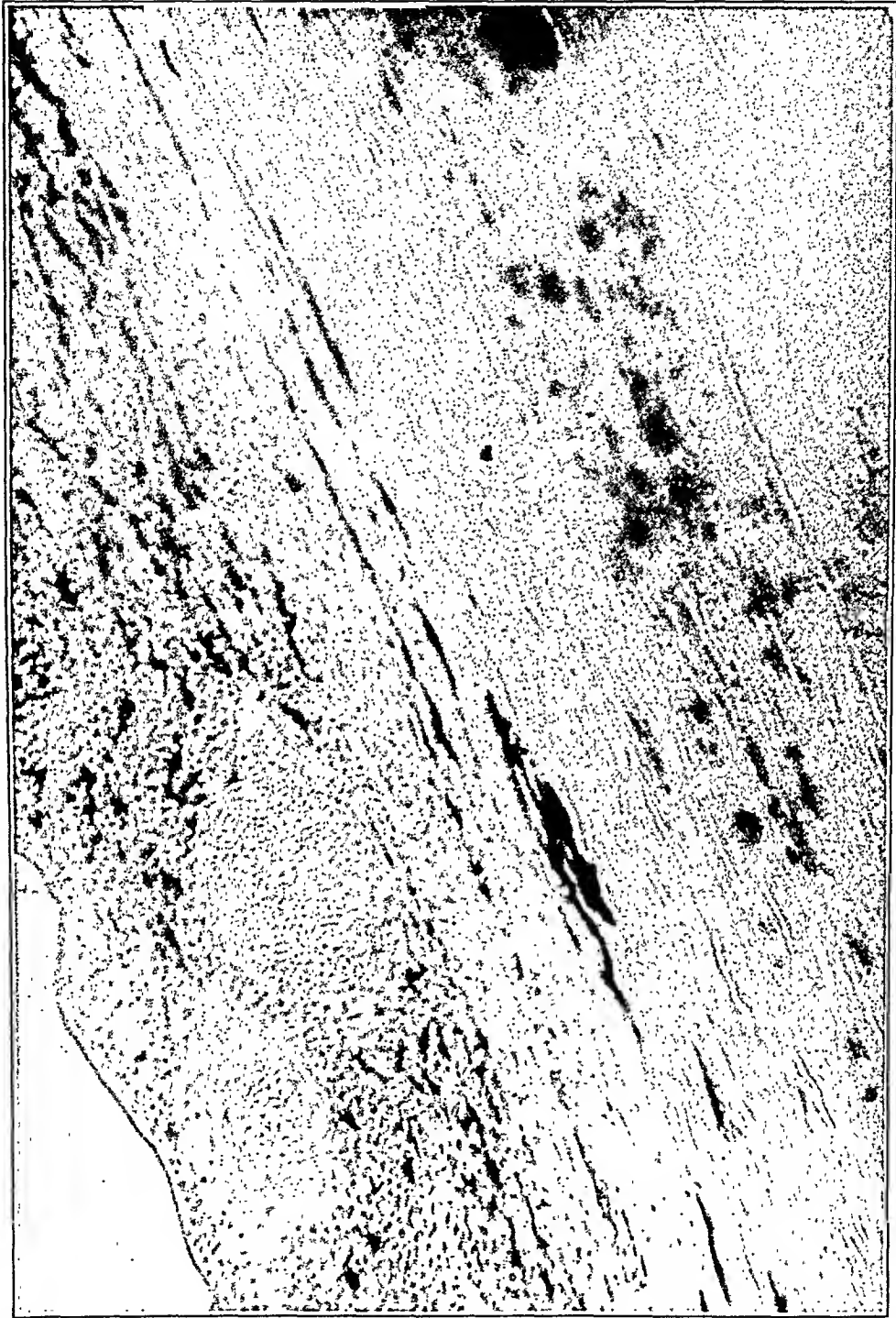


Fig. 3.—Section of choroid and sclera (X 100) in the posterior portion of the globe, showing infiltration of the choroid (chiefly by plasma cells) and calcification of the sclera.

surface. The anterior chamber was of normal depth but was filled with an eosinophilic coagulum containing fibrin and white blood cells, predominantly polymorphonuclear in type, but no giant cells. The angle of the anterior chamber was obliterated on one side by a 0.5 mm. anterior peripheral synechia and on the other side by a 1 mm. synechia; on the latter side, however, there was an open recess corresponding to the most peripheral portion of the chamber. Schlemm's canal, filled with blood, was discernible on both sides.

The iris was of approximately normal thickness but was moderately infiltrated with polymorphonuclear cells and round cells; the infiltration was considerable along the anterior surface of the iris and was especially pronounced along the posterior surface for a distance of 1 to 2 mm. from the root of the iris. Here

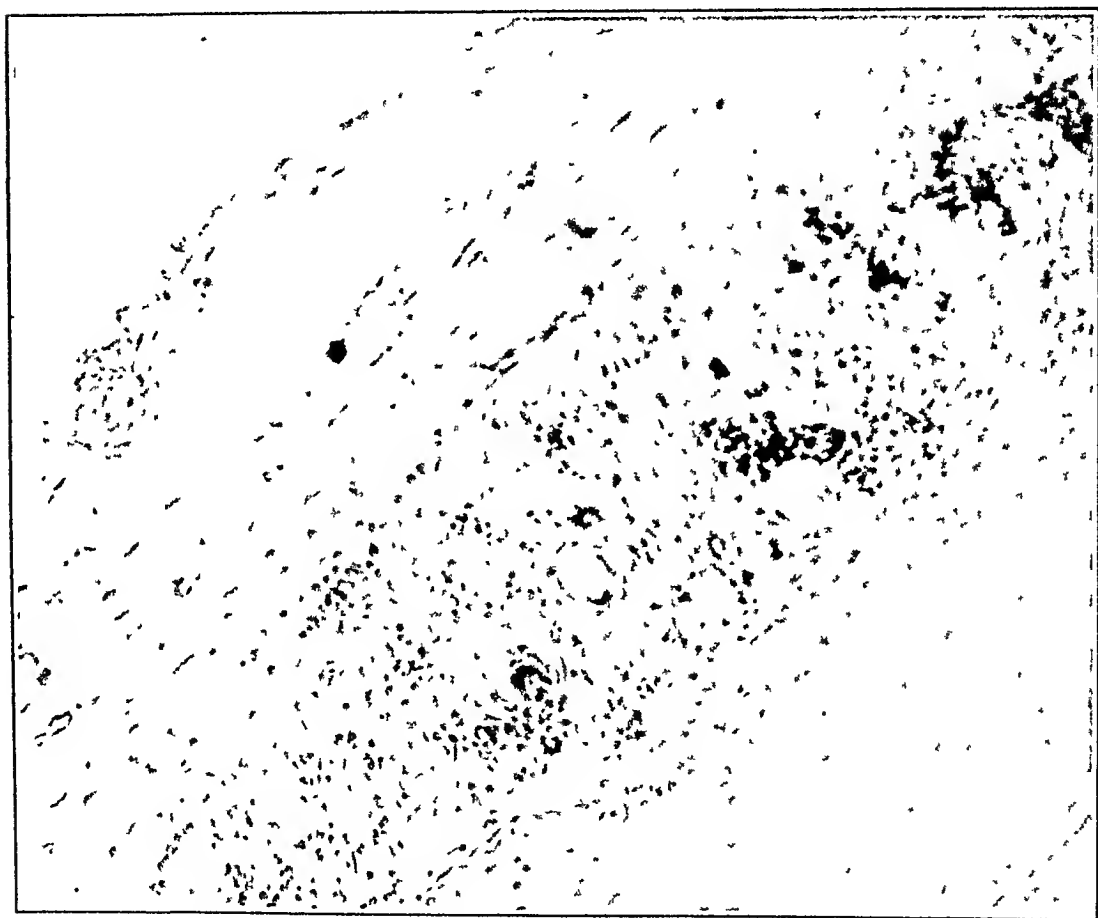


Fig. 4.—Mild infiltration of the inferior oblique muscle (by plasma cells) just behind the sclera ( $\times 100$ ).

the infiltrate had in some places broken through the pigment epithelium and joined with exudate in the posterior chamber (fig. 2). The infiltrate in the iris showed no predilection for the vicinity of the blood vessels. On the anterior surface of the iris on one side there was a new-formed membrane containing a blood vessel. The pupillary margin of the iris was bound to the lens by a seemingly firm posterior synechia with local disintegration of the pigment epithelium and, on one side, a backward displacement of the sphincter muscle (entropion uveae). The pupil itself was occluded by a connective tissue membrane 0.1 to 0.2 mm. thick, containing capillaries adjacent to the iris. Some sections showed the posterior part of this membrane to be undergoing a basophilic type of degeneration. The posterior chamber contained many pus cells with occasional macrophages,



fibroblasts, epithelioid cells and some fibrin. The epithelioid cells, many of which were multinucleate, were most abundant in the region of the ciliary body and gave the impression of being derived from its unpigmented epithelium; an occasional area was seen in which pyknotic nuclear material was contained within the cells of the ciliary epithelium in situ.

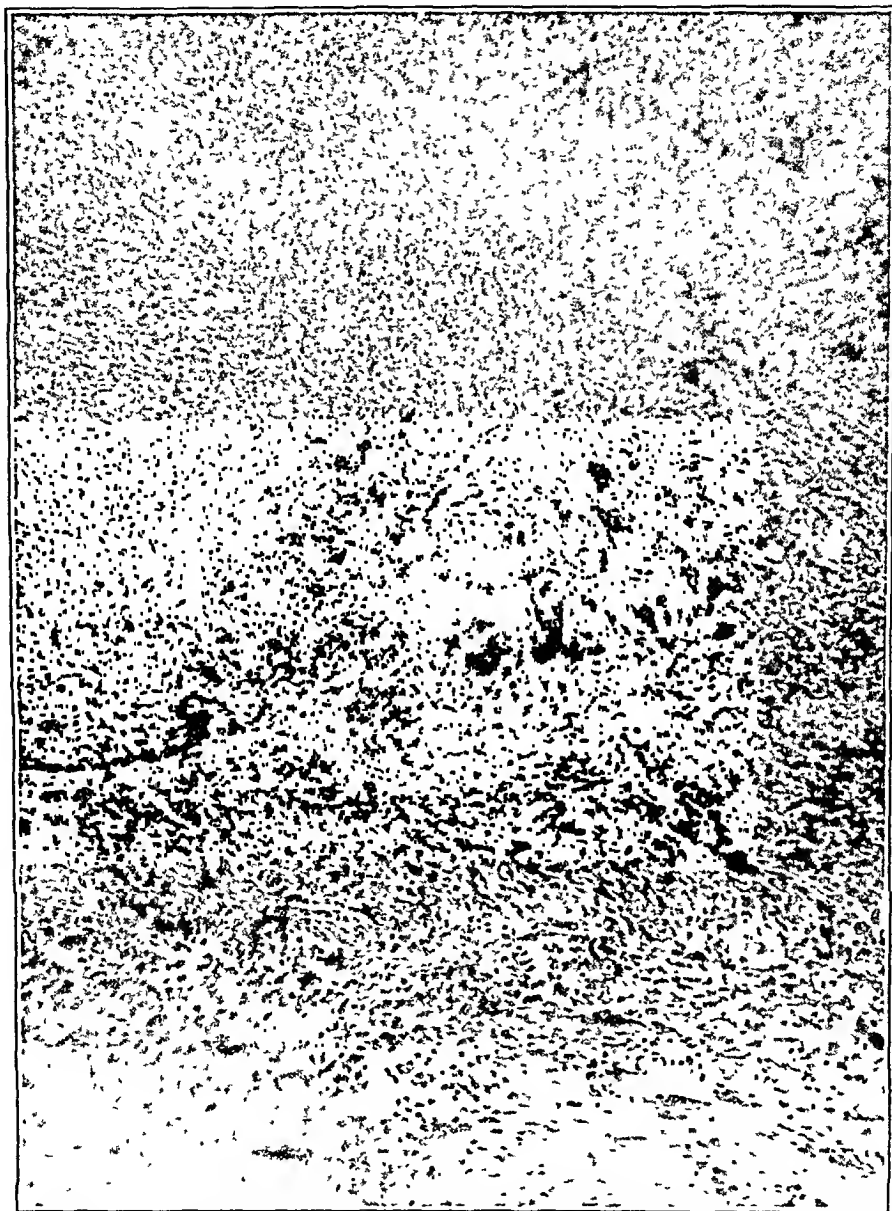


Fig. 5.—Dense spindle cells and a large giant cell separating the disorganized retina, in the lower part of figure, from the vitreous abscess, in the upper part of figure ( $\times 400$ ).

The lens was in place and showed a few morgagnian globules in its cortex but was otherwise normal.

Except for some infiltration, especially by plasma cells, some edema and hyalinization and calcification of its processes, the ciliary body was not remarkable.

Similarly, the only noteworthy changes in the choroid were edema and diffuse infiltration with plasma cells (fig. 3). Occasionally, however, the retina was fused with the choroid, and the pigment epithelium was locally destroyed. In one place an abscess from the retina had extended into the choroid, and in several



Fig. 6.—Giant cell which has been artificially separated from the abscess (left of figure), showing hyphae in the process of being phagocytosed ( $\times 1,000$ ).

places abscesses apparently continuous with those in the retina had lifted up the pigment epithelium.

The sclera was of normal thickness throughout, was free of infiltration but did show extensive calcification in the posterior half of the globe, especially about

the optic foramen. In the posterior portion of the eye the extraocular structures showed mild but definite infiltration with lymphocytes and plasma cells (fig. 4). This was especially evident in the portions of the oblique muscles and fat adherent to the globe. There were also some perivascular infiltration and obliterative changes in the smallest vessels.

The most significant changes were in the retina and vitreous. The retina was separated. It showed extensive edema and occasional hemorrhage, and, except for irregular persistence of the outer nuclear layer and some of the inner nuclear layer, the architecture was completely lost. The rods and cones had been com-

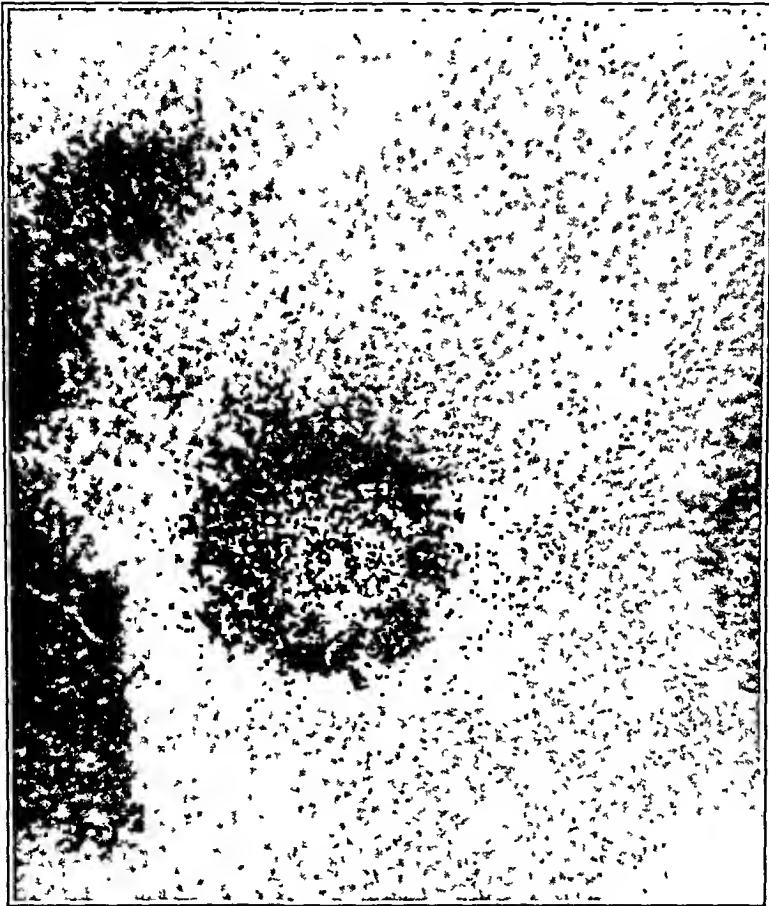


Fig. 7.—Small vitreous abscess containing a single hypha in its center ( $\times 100$ ).

pletely replaced by several laminas of connective tissue, to which the pigment epithelium was adherent. The innermost layer had been replaced by spindle cells, round cells (glia?) and purulent exudate. On the inner side of the retina and in the vitreous were multiple abscesses. The junction between infiltrated retina and vitreous abscess was usually abrupt, the former showing a dense membrane of spindle cells. In places these spindle cells projected into the vitreous between the abscesses, suggesting an attempt at encapsulation. Especially characteristic of the boundary between retina and abscesses was the presence of multinucleate giant cells, these cells being sometimes so numerous as to form distinct laminas (fig. 5). Some of these giant cells attained 0.1 mm. in diameter. The abscesses

tended to separate from the outer walls at the junction with the ganglion cells. Although this separation was an artefact incident to the sectioning, it was noted sufficiently often to suggest a potential line of cleavage here. It also served to

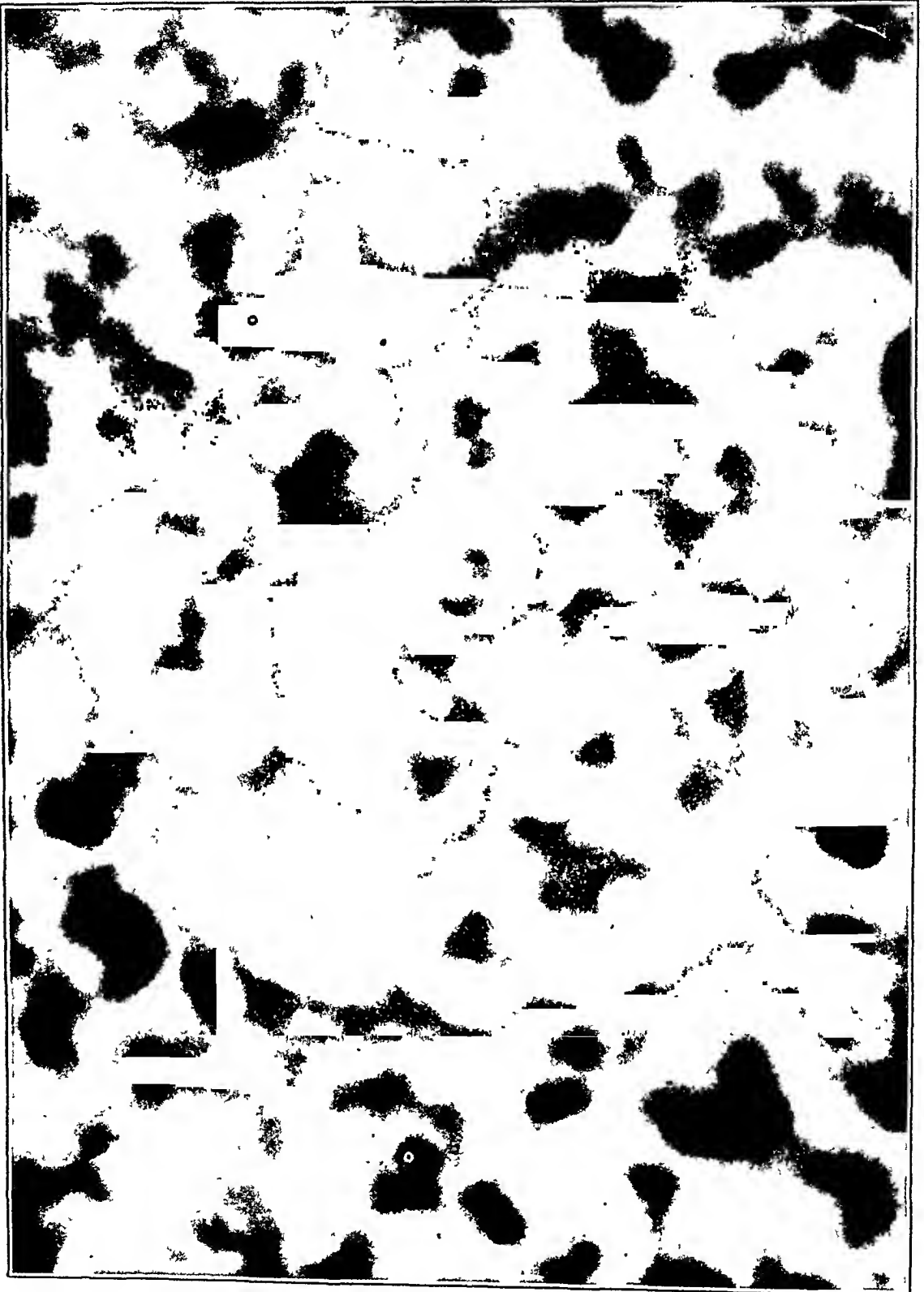


Fig. 8.—A higher magnification of the section shown in figure 7.

expose fungus particles that might otherwise have been hidden by the cellular exudate (fig. 6).

The posterior portion of the vitreous contained many small abscesses showing an occasional giant cell and many fungus organisms. The fungi tended to be centrally situated in the abscess and often surrounded a necrotic area. Frequently, a single fungus particle could be seen centrally in an abscess, surrounded by a relatively clear halo and a dark ring of cells (figs. 7 and 8). The abscesses were made up of pus cells, showing varying degrees of necrosis and occasionally

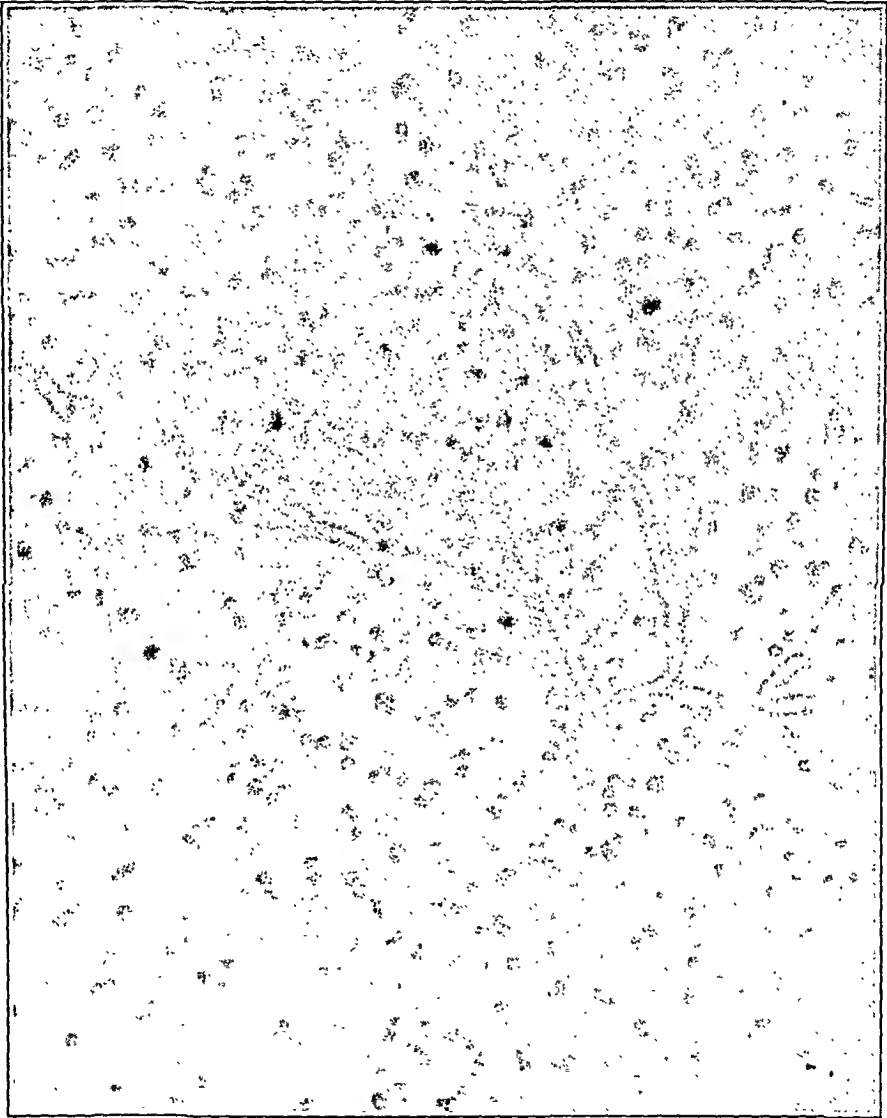


Fig. 9.—Smooth-walled fungus particles, consisting of cylindric tubes with dichotomous branches and blunt ends ( $\times 400$ ).

containing a giant cell. Eosinophils were rarely present. Solitary giant cells were occasionally to be seen free in the vitreous.

The fungi consisted of cylindric structures, measuring uniformly 3 microns in diameter and varying in length from 10 to 150 microns. The hyphae branched dichotomously (fig. 9). Transverse septums were rarely to be seen. The branch-

ing of the hyphae was Y shaped, and each arm of the branch had the same diameter as the stem from which it came. Usually there were not more than one or two branches for each hypha. Rarely did multiple branches come off the same place in the stem. The hyphae ended abruptly without tapering, budding or other evidence of differentiation. In the vicinity of the mycelium, and especially within its meshes, were circular, occasionally oval, bodies, measuring 3 to 4 microns in diameter and often having a thick wall (0.5 micron) and a clear, refractile center. These may have been spores but were more likely cross sections of hyphae. Both the hyphae and these circular bodies were to be seen occasionally within giant cells.

The hyphae had either clean-cut walls or fuzzy, corrugated walls but tended to be uniform for any one vicinity. The former were to be found where the

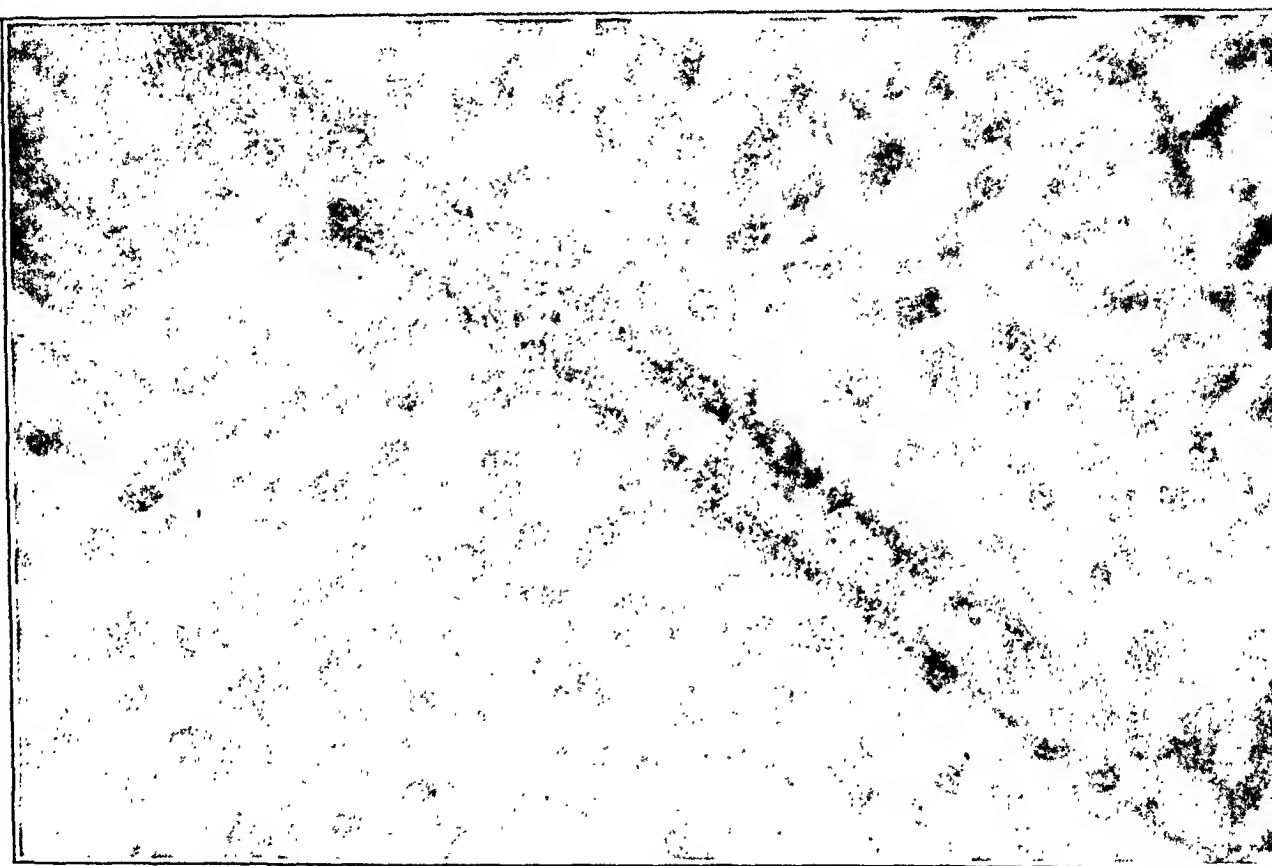


Fig. 10.—Excrescences attached to the wall of a hypha ( $\times 1,000$ ).

mycelium was especially abundant (rapidly growing?) and were more evident in the periphery of an abscess or in relatively cell-free areas, while the latter were to be found where the hyphae were present as short, isolated stalks (necrotic?) and were more evident in the center of an abscess.

The corrugations merit special comment. They varied from merely a pepper-like deposit on and in the vicinity of the hypha wall to gross, wartlike excrescences, obviously continuous with the wall (fig. 10). The former looked like an artefact, but the latter suggested lateral budding. This was especially true when the excrescences developed constricted necks at their point of attachment to the hypha stalk. However, these excrescences were characteristically irregular in size and shape and did not have the uniformity which one would expect if they represented true budding. They were definitely more abundant in hyphae that

were disintegrating and sometimes could be seen accompanying a fragmentation of a hypha stalk (fig. 11). With the Gram stain many such particles were to be seen in the vicinity of the fungus.

The fungus stained well with hematoxylin and could be readily seen with routine sections stained with hematoxylin and eosin or methylene blue. It was seen well also with the ordinary Gram stain, with Verhoeff's modified Gram stain and, especially, with thionine. The hyphae containing the excrescences on their walls stained much more intensely than did the cleancut hyphae. The organism stained either positively or negatively with the Gram method, depending on the intensity of the stain, but the stalk of the hypha tended to be gram-negative

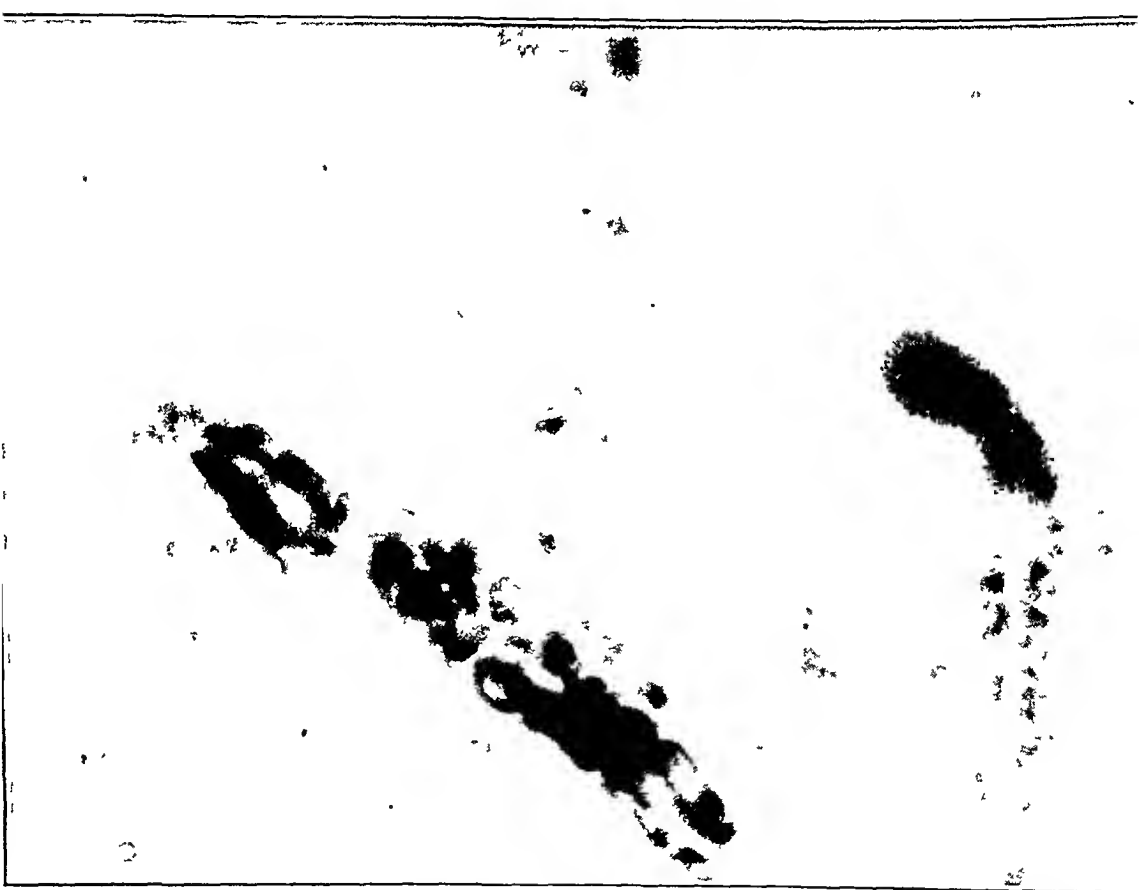


Fig. 11.—Large, wartlike excrescences with apparent fragmentation of the hypha ( $\times 1,000$ ).

while the excrescences were gram-positive. The organism was not carbolfuchsin fast. No bacteria or other organisms were noted in any of the sections.

Especially noteworthy was the presence of yellowish brown pigment granules frequently associated with the fungus mycelium. The granules were of the same size and could not be differentiated histologically from those of the pigment epithelium. Although occasionally scattered in random fashion, the pigment granules were for the most part aggregated in spherical bodies without any capsule or other evident means of cohesion. They were to be found exclusively where the fungous mycelium was especially dense and made up of clear-walled hyphae,

as though rapidly growing. Yet the pigmented granules were most evident on the periphery, and not within the densest part of the mycelium. Especially striking was a line of mycelium and pigment granules (fig. 12), suggesting that the pigment was in fact derived from the pigment epithelium. Yet no nuclear or other cellular structure could be identified with the pigment, nor is it apparent why the mycelium should form a compact mass associated with the pigment

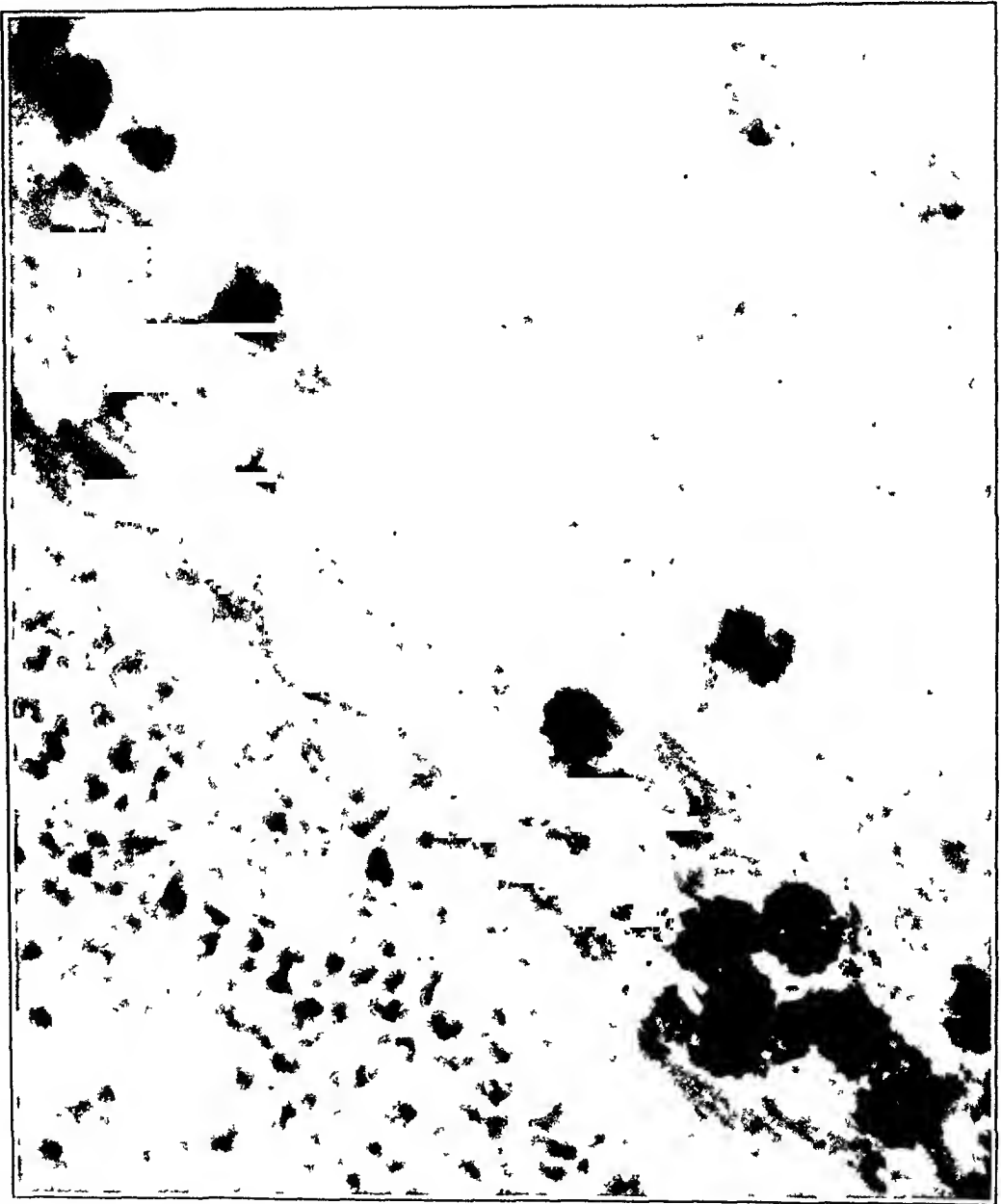


Fig. 12.—Mycelium bordering a collection of pus cells but growing freely into the vitreous and containing within its meshes spheres of pigment granules ( $\times 1,000$ ).

epithelium. Some fields showed the pigment granules in the periphery of the mycelium not arranged in linear fashion. These fields are what one might expect in a tissue culture and, significantly, were to be seen only in relatively cell-free areas in the vitreous.

No organisms were observed in the anterior chamber, uvea or extraocular structures, the fungi being entirely limited to the vitreous and retina.



## COMMENT

To attribute the cause of the abscesses in the present case to primary fungous infection, one must exclude, first, the possibility that the fungi occurred in the tissues as the result of postenucleation contamination and, second, the possibility that the fungi might have been secondary invaders of the eye before enucleation.

The first possibility is unquestionably disproved by the restricted localization of the fungi in the region of the abscesses and by the active phagocytosis of the fungi by giant cells. The second possibility—that the fungus was secondary to some other pyogenic excitant—cannot be disproved with certainty, but it seems most unlikely in view of (1) the nature of the granuloma, (2) the predominant orientation of the fungi within the abscesses and (3) the absence of other organisms.

Identification of the fungus must be open to question in the absence of data regarding its cultural characteristics; however, it does not appear to have been one of the common pathogenic organisms. Actinomycosis is ruled out by the absence of ray myceliums. Blastomycosis, coccidiosis and rhinosporidiosis are ruled out by the presence of a mycelium and by the absence of endospores. Histoplasmosis is ruled out by the absence of the organisms in lymph and blood vessels. The hyphae in the present case were too large to be those of *Sporotrichum* or *Candida* and too small and too regular to be those of *Mucor*. The remaining possibilities by exclusion are *Aspergillus*, which has been responsible for numerous ocular infections after perforating injuries, or some organism not ordinarily thought to be pathogenic, such as *Penicillium* or *Hormodendron*.<sup>14</sup>

The fungus in the present case appears to be identical with that found by Dimmer<sup>2</sup> in an eye with choroidoscleritis and by Stock,<sup>3</sup> Archangelsky,<sup>9</sup> Rohner and Huber<sup>10</sup> and Lorenz<sup>11</sup> in the eyes with

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14. Specimens were submitted to two mycologists, and their opinions follow: Jacob Schwartz, M. D. (Harvard University) wrote: "[The specimens] show rather coarse hyphae with and without branching, both septate and nonseptate, mostly septate. There are spores, both free and attached. In one instance a broomstick-like arrangement of hyphae and spores suggests *Penicillium*. In several instances the arrangement of hyphae and spores suggests the genus *Hormodendron*. I cannot specifically identify the fungus."

Norman F. Conant, Ph.D. (Duke University): "There are indeed some branching hyphae in the abscess. It is not possible, however, to identify the fungus."

retinovitreal abscesses. All described the fungus as being approximately the same size as stated here and as having cylindric hyphae with dichotomous branching and rare, if any, septums. No definite fructification bodies were seen, and no cultures were made; but all authors stated the belief that the organism was *A. fumigatus*. The illustrations in their reports leave little doubt as to the morphologic identity of the fungus in these 5 cases, one with another, and with known aspergillus infections of the ocular tissues following perforating wounds<sup>15</sup> or experimental inoculations.<sup>16</sup> The unusual features of the case here reported are (1) the presence of fungus particles within giant cells, a finding not heretofore noted; (2) the presence of lateral excrescences on the walls of the hyphae, an observation noted previously once but interpreted as lateral budding, whereas the interpretation here suggested is that the excrescences are a product of disintegration of the fungus, and (3) the presence of pigment granules where the fungus is most freely growing.

These 6 cases also had clinical and pathologic features which were similar one with another and yet different from those in the other 6 cases of endogenous intraocular fungous infection, caused by an actinomycete-like organism or by blastomycetes. In only 1 of the former cases was there a systemic condition suggesting the source of the fungus, and this merely bronchitis, whereas of the 3 cases of actinomycetic infection the ocular condition followed a febrile illness in 1, was associated with frank actinomycosis of the lungs in another and followed an operation on the fellow eye in the third, and of all the cases of blastomycotic infection of the eye the condition was associated with generalized blastomycosis.

#### SUMMARY

Eleven cases of endogenous intraocular fungous infection have previously been reported. Of these, the causative organism was blastomycete in 3 cases, an actinomycete-like organism in 3 cases and a cylindric branching fungus thought to be *A. fumigatus* in 5 cases. In the present report an additional case apparently belonging to the aspergillus group is described. The onset was characterized by loss of vision, redness, chemosis and proptosis, without any evidence of systemic disease. The tension, which was low at first, became elevated, and

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15. Rychener, R. O.: Intra-Ocular Mycosis, Tr. Am. Ophth. Soc. **31**:477, 1933.

16. An excellent summary of aspergillus infection of the eye may be found in Rohner and Huber.<sup>10</sup>

the eye was removed on account of pain. Histologically the significant feature was the presence of abscesses, with many giant cells in the vitreous and in the inner portion of the retina. In the vicinity of the abscesses, often within their centers, were the fungus particles, consisting of cylindric bodies having a dichotomous type of branching and rare septums. Excrescences on the walls of these hyphae were interpreted as manifestations of disintegration.

243 Charles Street (14).

## News and Notes

EDITED BY DR. W. L. BENEDICT

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### GENERAL NEWS

**National Foundation for Eye Research.**—An organization known as the National Foundation for Eye Research, founded in Washington, D. C., and with offices in the Shoreham Building, proposes to raise funds for ophthalmic research. This Foundation hopes to encourage public support for medical research aimed at discovering the causes of and developing more efficacious therapies for ocular diseases leading to blindness.

The National Foundation for Eye Research will differ in its operation from many organizations designed to further medical research in that its funds will not be restricted to the study of any one disease but will be used to promote research in the whole field of ophthalmic diseases.

The activities of the Foundation will be limited entirely to supporting and establishing research centers for ophthalmology in various localities, leaving other approaches to the prevention of blindness and the rehabilitation of the blind to existing agencies.

The need for an expanded research program is apparent when one considers that there are about 260,000 blind persons in the United States, with 20,000 new cases added annually, and that the existing funds, facilities and personnel available for ophthalmic research are pitifully inadequate to study thoroughly the basic causes of the diseases which result in blindness. For instance, there is less than \$400,000 spent annually in the United States on medical research primarily designed to decrease the number of blind—less than 1 per cent of that used for rehabilitation of persons who have already lost their sight. Moreover, there are only about a dozen trained, full time research men working in this field in the whole country, and few practicing ophthalmologists can devote a significant amount of time to research because of the restrictions of an active practice.

Mr. George Swartz, well known for his promotion of other medical philanthropies, has been selected as national chairman. With the assistance of a board of directors composed of prominent laymen, he will be responsible for the activities related to raising the necessary funds. The allocation of funds for research purposes will be made on the advice of a scientific advisory board, consisting of Dr. V. Everett Kinsey (chairman), Dr. Francis Heed Adler, Dr. Edwin B. Dunphy, Dr. Jonas Friedenwald, and Dr. Alan C. Woods. It is proposed to add several members to the board as the need for expansion arises.

It is hoped that ophthalmologists through their contact with the public will add their support to this group of laymen whose interest in expanding ophthalmic research has led to the formation of the National Foundation for Eye Research.

**Third Annual Clinical Session of the American Medical Association.**—The Third Annual Clinical Session of the American Medical Association will be held in Washington, D. C., December 6 to 9.

The Clinical Session will provide a full scale scientific program specifically designed for the general practitioner. Outstanding physicians will discuss such subjects as diabetes, pediatrics, laboratory diagnosis, physical medicine and rehabilitation, arthritis, dermatology, roentgen ray diagnosis, cancer and poliomyelitis. Coordinated with this notable scientific program will be approximately one hundred scientific exhibits which will present original work on the subjects discussed.

The newest offerings of one hundred and twenty-five manufacturing firms will comprise the Technical Exposition. Here will be found the latest developments in scientific medical research, drugs and equipment.

Televised surgical and clinical procedures, similar to those shown in color at the Annual Session of the American Medical Association in Atlantic City last June, will be presented at the Washington meeting. The demonstrations will originate in the Johns Hopkins Hospital and will be shown on screens in the Armory. The television schedule will be spread over four days.

The House of Delegates will meet at the Hotel Statler during this session. One of the first orders of business will be the annual selection of the general practitioner who has made an exceptional contribution of service to his community.

An entertainment program for attending physicians and their wives is being planned. The highlight of this program will be on Wednesday evening, December 7, when Philip Morris' "This is Your Life" will be broadcast from the Hotel Statler. The radio program will be followed by a stage show, in which outstanding stars will participate.

Blanks for hotel reservations and advance registrations may be found in *The Journal of the American Medical Association*.

**Refresher Course in Ophthalmology and Otolaryngology, University of Toronto Faculty of Medicine.**—The University of Toronto Faculty of Medicine offers a combined refresher course in ophthalmology and otolaryngology from Jan. 9 to Jan. 14, 1950.

The otolaryngologic subjects will be presented during the first three days of the course, and the ophthalmologic subjects, during the last three days. Lectures and surgical clinics in both fields will be given by outstanding guest speakers, as well as by members of the Faculty.

Guest Speakers are: Dr. W. J. McNally, Montreal, and Dr. Henry Orton, Newark, N. J., in otolaryngology, and Dr. P. C. Kronfeld, Chicago, and Dr. J. A. MacMillan, Montreal, in ophthalmology.

The course will be given for a minimum of 10 students and a maximum of 20 students. The fee for all or any part of the course will be \$100, payable to the chief accountant, Simcoe Hall, University of Toronto.

Application should be made to the Dean of the Faculty of Medicine, not later than Nov. 30, 1949.

# ARCHIVES OF OPHTHALMOLOGY

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## AN OPERATION FOR PTOSIS UTILIZING THE SUPERIOR RECTUS MUSCLE

R. N. BERKE, M.D. .  
HACKENSACK, N. J.

**I**N VIEW of the fact that more than eighty operations have been proposed for the treatment of ptosis, there would seem to be little justification for sponsoring another. However, it might be argued that the large number of procedures already available is adequate proof that none is eminently successful in all cases. For example, resection of the levator palpebrae superioris usually results in failure when levator action is absent; suspension of the upper lid from the brow produces lagophthalmos in looking down, while utilization of the superior rectus muscle causes a notch in the lid or hypotropia or both. It is obvious, therefore, that none of these procedures can give a satisfactory result in all cases. This is especially true of complete ptosis, i. e., complete paralysis of the levator.

### OPERATION FOR PTOSIS UTILIZING SUPERIOR RECTUS MUSCLE

#### INDICATIONS FOR OPERATION

The operation proposed here is not recommended for all types of ptosis but is designed only for those cases in which resection of the levator palpebrae is not indicated.<sup>1</sup> Specifically, this operation is useful in four types of ptosis: (1) complete ptosis<sup>2</sup> with normal superior rectus muscles, (2) complete ptosis with weak superior rectus muscles, (3) ptosis associated with the jaw-winking phenomenon of Marcus Gunn and (4) complete ptosis associated with blepharophimosis.

*Complete Ptosis with Normal Superior Rectus Muscle.*—In a recent survey<sup>3</sup> of 200 cases of congenital ptosis, it was shown that in 74 per cent of the 200 cases normal superior rectus muscles were associated with absence of levator action. Cases of this type are considered by some

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1. In more than 50 per cent of cases of congenital ptosis levator action is sufficient to warrant resection of the levator muscle as the operation of choice.

2. By complete ptosis I mean ptosis with no levator action present. This condition is characterized by absence of elevation of the upper lid in looking up, by lack of an upper lid fold and by narrowing of the palpebral fissure in looking up.

3. Berke, R. N.: Congenital Ptosis: A Classification of Two Hundred Cases, Arch. Ophth. 41:188-197 (Feb.) 1949.

surgeons to be ideal for the Motaïs-Parinaud operation, this operation being based on the assumption that a normal superior rectus muscle can raise both the globe and the upper lid without complication. That a normal superior rectus cannot perform this dual task satisfactorily was demonstrated in a study of the postoperative results in 35 cases in which the Motaïs-Parinaud operation was done.<sup>4</sup> In at least 75 per cent of the cases postoperative hypotropia developed because of weakness of the superior rectus induced by the operation. Therefore, if utilization of the lifting power of a normal superior rectus muscle to correct ptosis induces a weakness of this muscle, it would seem logical to foresee this complication and to shorten the muscle to increase its lifting power when doing this operation for ptosis. The operation described here was designed to meet this need. It is a modified Motaïs procedure and consists in a combination of two operations: an operation on the globe to shorten the superior rectus, combined with suspension of the lid from the superior rectus muscle to correct ptosis.

Most ophthalmologists avoid operations on the superior rectus muscle because such operations are seldom indicated and the results, as reported in the literature, are variable and confusing. One would expect that a 5 to 6 mm. resection of a normal superior rectus muscle, as recommended in the operation for ptosis presented here, would tend to produce overaction of this muscle, with troublesome postoperative diplopia. However, this does not occur because the added weight of the lid counterbalances this tendency. Therefore, when performing the operation advocated here, the surgeon need not feel any anxiety regarding the resulting diplopia or a disfiguring hypertropia. I have done this operation four times on a normal superior rectus muscle without inducing overaction or diplopia in a single case (cases 1 to 4).

*Complete Ptosis with Weak Superior Rectus Muscle.*—In the report<sup>3</sup> previously referred to, it was further shown that in about 18 per cent of the 200 cases complete ptosis was combined with a weak superior rectus muscle. This type presents a difficult surgical problem because, in the absence of levator action, resection of the levator muscle usually results in failure, and because the Motaïs-Parinaud operation, done on an already weak superior rectus muscle, only increases the hypotropia present. For these reasons, Wiener<sup>5</sup> advocated the operation utilizing the frontalis muscle in such cases. On the other hand, Wheeler<sup>6</sup> avoided doing the frontalis muscle operation because of the unsatisfactory cosmetic and functional results obtained. Instead, he resected the

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4. Berke, R. N.: Motaïs-Parinaud Type of Operation for Ptosis, *Arch. Ophth.* **41**:324-333 (March) 1949.

5. Wiener, M.: Surgical Correction of Ocular Disfigurements, *Surg., Gynec. & Obst.* **58**:390-393, 1934.

6. Wheeler, J. M.: Correction of Ptosis by Attachment of Strip of Orbicularis Muscle to Superior Rectus Muscle, *Arch. Ophth.* **21**:1-7 (Jan.) 1939.

superior rectus and/or the inferior oblique as indicated to elevate the globe and at a later date performed a Moutais operation to correct the ptosis. After a few unhappy experiences with this plan, Kirby<sup>7</sup> advocated the frontalis muscle operation. White<sup>8</sup> insisted, however, that the hypotropia should be remedied before the ptosis was corrected.

I have performed the present operation ten times on eyes with weak superior rectus muscles, with improvement in the ptosis and the hypotropia in every case (cases 5 to 14).

*Ptosis with the Jaw-Winking Phenomenon.*—In about 6 per cent<sup>3</sup> of all cases of congenital ptosis the jaw-winking phenomenon of Marcus Gunn is present, in some with and in some without normal ocular elevation. The ptosis here is always unilateral and may be complete or incomplete. The most characteristic feature, the jaw-winking phenomenon, is brought out when the mandible is depressed, as in eating, or when it is moved to the side opposite the ptosis. When the jaw is in either of these two positions, the upper lid of the affected side moves upward, sometimes higher than the lid on the sound side, especially when the eyes are directed down.

When the superior rectus is weak in a case of the jaw-winking phenomenon, one must elevate the globe, correct the ptosis and abolish the jaw-winking reflex. These three objectives can be achieved in one sitting by the operation described here. First, the jaw-winking phenomenon is abolished by excising a strip of the tendon of the levator muscle thus converting what is usually an intermittent, incomplete ptosis into a complete one. Then the superior rectus is shortened to correct the hypotropia, and, at the same time, the ptosis is corrected by the operation described here. This procedure, performed in 5 cases, has been followed with a good result in each case (cases 15 to 19).

*Ptosis Associated with Blepharophimosis.*—This type of ptosis comprises about 3 per cent of all cases of congenital ptosis<sup>3</sup> and is characterized by abnormally short palpebral fissures, a great intercanthal distance over the bridge of the nose between the inner canthi and ptosis. In about 60 per cent<sup>3</sup> of these cases enough levator action is present to justify resection of the levator muscle. In the other 40 per cent the ptosis must be corrected by utilizing the lifting power of either the superior rectus or the frontalis muscle.

Before correcting the ptosis, the blepharophimosis and the abnormally great distance between the inner canthi must be remedied. The

7. Kirby, D. B.: Paralysis of Ocular Elevation With and Without Ptosis, Tr. Am. Ophth. Soc. 43:218-239, 1945; Arch. Ophth. 35:199-217 (March) 1946.

8. White, J. W.: Choice of Fixating Eye in Paralytic and Non-Paralytic Strabismus, Am. J. Ophth. 27:817-819 (Aug.) 1944; Paralysis of the Superior Rectus and the Inferior Oblique Muscles in the Same Eye, Arch. Ophth. 27:366-371 (Feb.) 1942.

palpebral fissures can be lengthened by an external canthoplasty, and the distance between the inner canthi can be decreased by shortening the inner and tenotomizing the outer canthal ligaments. This plan of procedure was followed in 1 case with a fairly good result (case 20)

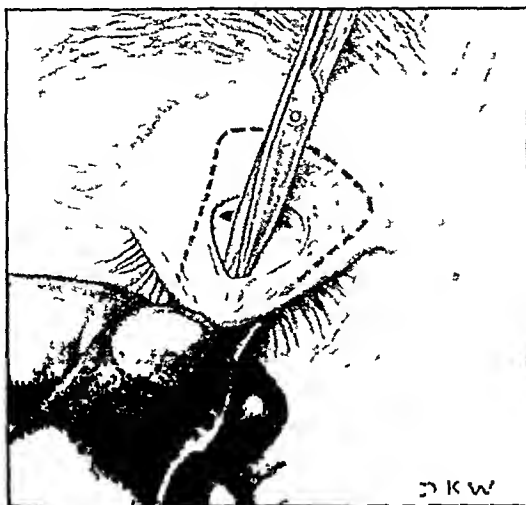


Fig. 1.—An incision 20 to 25 mm. long has been made through the skin and orbicularis muscle. A horn plate is used to support the lid while the skin and orbicularis are reflected down to the cilia. The incision through the conjunctiva above the tarsus can be seen behind the scissors.

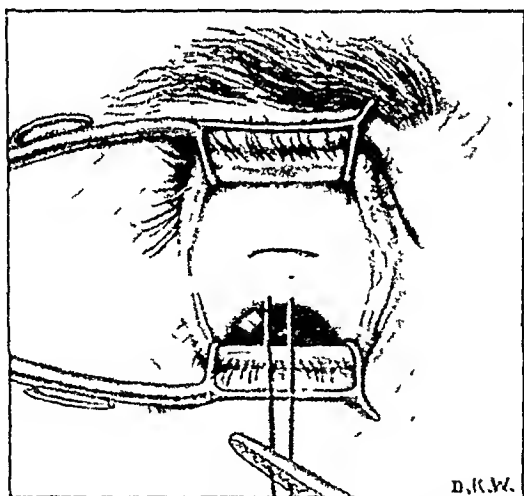


Fig. 2.—A traction suture has been passed through the limbus to pull the globe down, and an incision is made through the conjunctiva over the insertion of the superior rectus muscle

#### TECHNIC OF OPERATION

1. With the patient under general anesthesia, an incision is made through the skin and the orbicularis muscle of the upper lid for a distance of 25 mm. exactly where the upper lid fold should be to match that of the fellow eye

2. The lower part of the skin flap with the orbicularis fibers is reflected from the tarsus down to the lashes and the upper portion of the flap is reflected upward to the upper edge of the tarsus. Here, an incision 10 mm. wide is made through the conjunctiva into the conjunctival sac (fig. 1).

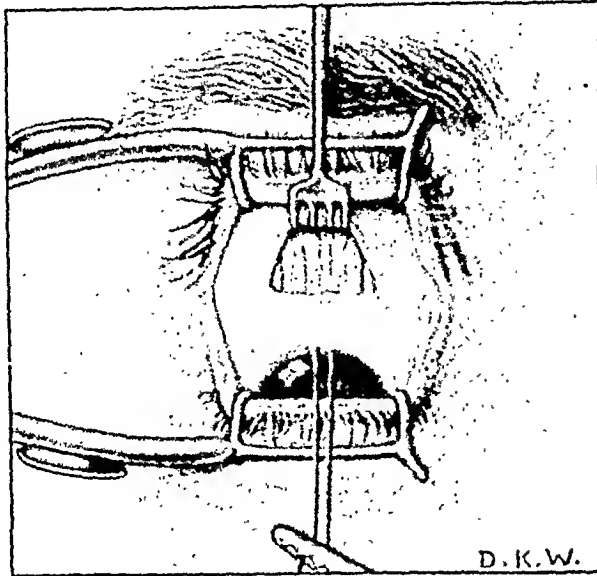


Fig. 3.—The superior rectus is exposed and freed from Tenon's capsule for a distance of 6 to 10 mm., care being taken not to sever the reflected tendon of the superior oblique muscle, which lies directly under it.

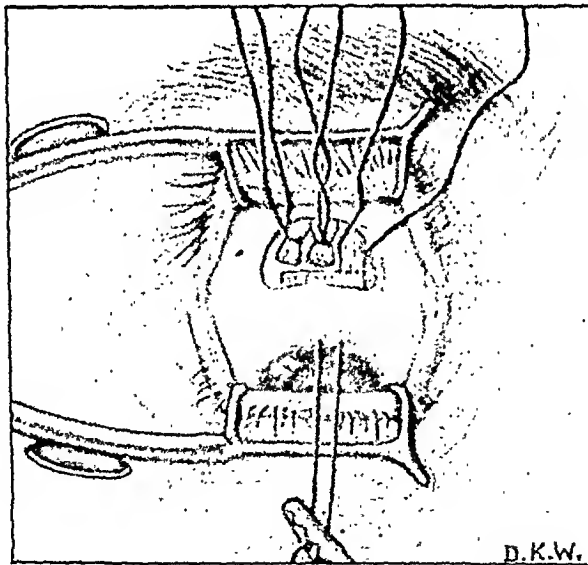


Fig. 4.—Three double-armed atraumatic 0000 plain surgical gut sutures are passed through the lateral, the middle and the medial third of the superior rectus tendon 2 or 3 mm. from its insertion and tied, leaving 2 mm. of tendon anterior to each knot. This may be done with or without the aid of a muscle clamp. If a muscle clamp is used in resecting the superior rectus, then it is more convenient to place these sutures after the muscle has been resected.

3. A speculum is then inserted, the globe pulled down by a silk suture inserted through the limbus at 12 o'clock and an incision made through the conjunctiva over the insertion of the superior rectus muscle (fig. 2).



4. After the superior rectus muscle has been exposed for 8 to 10 mm. posteriorly (fig. 3), three double-armed, plain 0000 surgical gut sutures are passed through the medial, the middle and the lateral third of the superior rectus

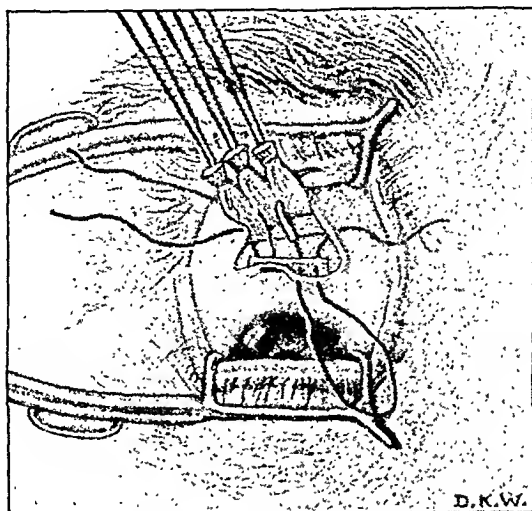


Fig. 5.—After the superior rectus is severed from the globe (with or without the aid of a muscle clamp) two double-armed 0000 chromic surgical gut sutures are passed first through the lower lip of the conjunctiva, then through the muscle stump attached to the sclera, then through the superior rectus at the proper height and, finally, through the upper lip of the conjunctiva and tied. Note the tendon of the superior oblique under the superior rectus muscle.

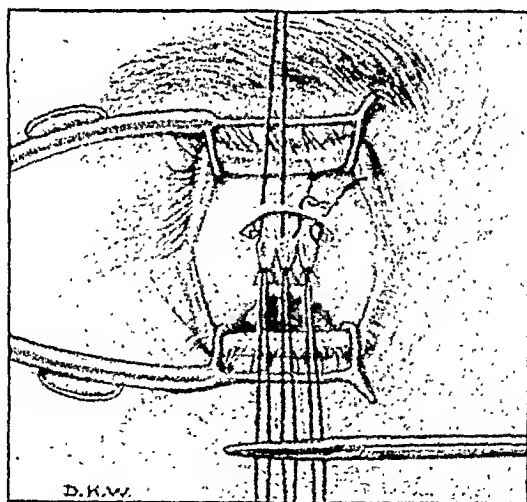


Fig. 6.—The two double-armed chromic surgical gut sutures, are tied, leaving exposed the three tongues of the superior rectus muscle.

tendon and tied to leave a 2 mm. stump anterior to the sutures (fig. 4). This may be done with or without the aid of a muscle clamp.

5. The tendon of the superior rectus muscle is then severed from the globe and the muscle shortened 5 to 10 mm. (depending on the weakness of the muscle) by passing two double-armed 0000 chromic surgical gut sutures first through

the lower lip of the conjunctiva (fig. 5), then through the muscle stump attached to the sclera, then through the superior rectus at the proper height and, finally, through the upper lip of the conjunctiva. When tied, these sutures close the conjunctival wound, effect a shortening of the superior rectus and leave an exposed tongue of muscle 5 to 10 mm. long (fig. 6).

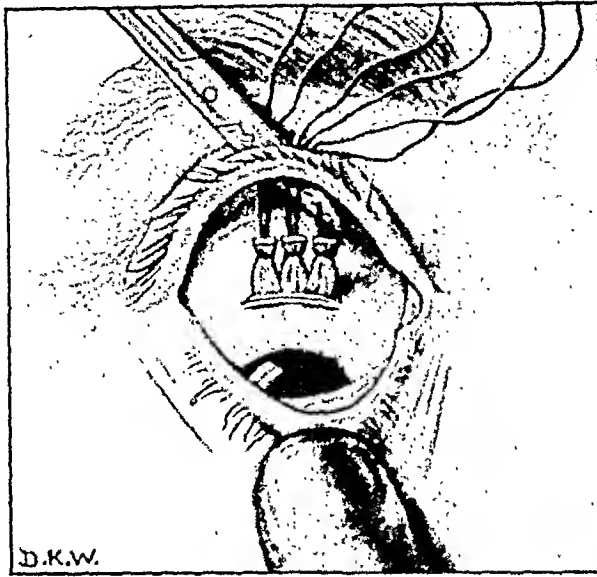


Fig. 7.—The three tongues of the superior rectus muscle are pulled forward through the previously made incision in the conjunctiva to the anterior surface of the tarsus.

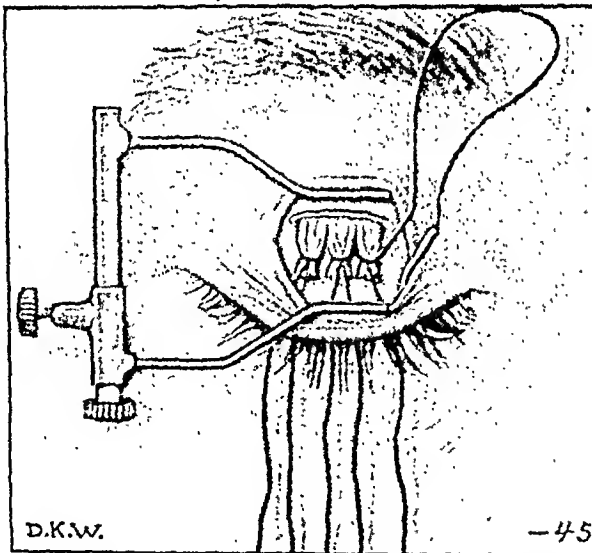


Fig. 8.—The three tongues of the superior rectus muscle are spread out on the anterior surface of the tarsus, and the three double-armed sutures are passed through the gray line of the upper lid so that each set of sutures is 5 to 6 mm. apart.

6. The exposed tongue of the superior rectus is then split into three smaller tongues, corresponding to the three previously placed plain surgical gut sutures, and pulled through the opening in the conjunctiva (fig. 7) on to the anterior surface of the tarsus, where the transplanted muscle tongues are spread out (fig. 8).

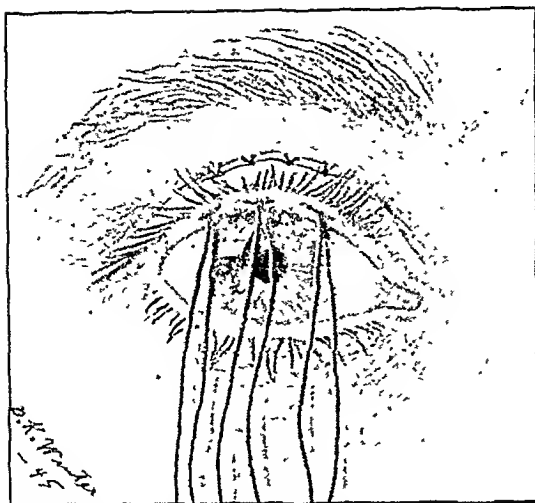


Fig. 9.—Each of the three double-armed sutures is tied with one knot to study the effect. When the lid has been elevated to the proper height and the curve of the upper lid has been adjusted to match that of the opposite eye, a second knot is tied and the sutures are cut short. Then three or four sutures are passed through the skin and under the transplanted tongue of the superior rectus as illustrated in figure 10. When tied, these sutures anchor the skin to the transplanted tongue, prevent entropion and create a natural-appearing upper lid fold.

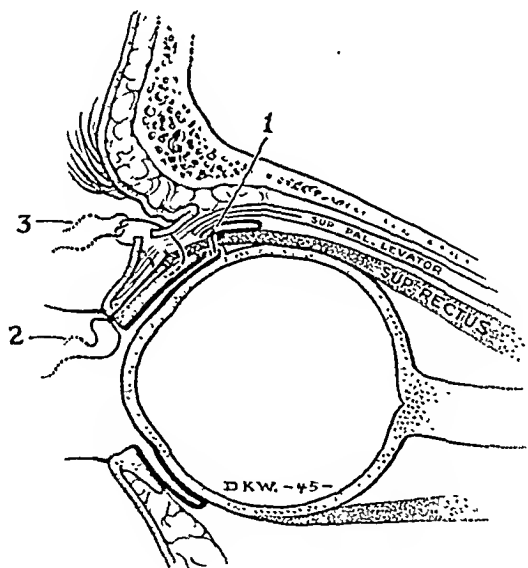


Fig. 10.—Sagittal section of the lids and globe illustrates the position of the three sets of sutures:

- (1) The two chromic surgical gut sutures which shorten the superior rectus and close the conjunctival wound;
- (2) the three plain surgical gut sutures which anchor the transplanted tongues of the superior rectus to the anterior surface of the tarsus;
- (3) the sutures (silk or gut) which close the skin wound, produce an upper lid fold and support the skin and lashes, thus preventing entropion.

7. The six needles of the three double-armed surgical gut sutures are then passed between the orbicularis and the tarsus through the gray line of the upper lid, so that each pair of sutures is 5 or 6 mm. apart (fig. 8). The sutures should not be passed through the lashes, else the lashes may grow distorted after operation.

8. The three sets of sutures are tied with one knot at first to permit a study of the effect. When the lid margin has been adjusted to the proper height and curve to match that of the fellow eye, a second knot is tied (fig. 9) and the sutures are cut short. An overcorrection of 2 mm. is necessary to counteract the postoperative reaction.

9. The skin wound is closed by means of three or more 000000 silk sutures (0000 plain surgical gut sutures in children), passed first through the lower skin flap, then under the three transplanted tongues of the superior rectus and, finally, through the upper skin flap (fig. 10). When tied, these sutures produce a natural-appearing upper lid fold and anchor the skin to the transplanted tongues of the superior rectus, thus preventing the lashes from turning in against the cornea.

10. The suture in the limbus is now removed; a Frost silk suture is passed through the lower lid, and the latter is pulled up to cover the cornea.

11. A petrolatum gauze dressing is applied with moderate pressure to keep down the edema.

#### AFTER-TREATMENT

The dressing and the Frost suture are removed on the fifth day, at which time the surgical gut sutures in the skin and lid margin are generally absorbed, leaving a natural-appearing lid margin and upper lid fold. It is important to protect the cornea against drying or injury for the first few days after removal of the dressing, for these corneas are more sensitive to exposure than normal corneas, having always been covered by the upper lid and never before having been completely exposed to the air. Unless these corneas are tested once a day with fluorescein and examined under the slit lamp, superficial staining and irritation may be permitted to develop. This condition can always be prevented if an anti-drying agent, such as 1 per cent methyl cellulose, is instilled into the conjunctival sac three or four times a day and again at bedtime. If staining should develop in spite of this precaution, it may be necessary to pull the lower lid up over the cornea by a strip of adhesive plaster at night. After a few weeks, this precaution and use of the methyl cellulose drops can be discontinued.

#### ADVANTAGES AND DISADVANTAGES

The operation presents the following advantages:

1. The superior rectus muscle can be used even though it is paralyzed.
2. Slipping of the transplanted muscle tongue is reduced to a minimum, thus assuring success oftener.
3. A smooth curve of the upper lid results, thus eliminating the notch so often produced by the classic Moutais procedure.
4. Entropion, or turning in of the lashes, of the upper lid is prevented.
5. A good upper lid fold, matching that of the fellow eye, is produced.

6. Postoperative hypotropia is prevented or greatly reduced.
7. The operation can be used even for very young children because the entire width of the superior rectus muscle is used.
8. The lid moves up and down synchronously with the globe.
9. The operation is tedious and exacting, but not difficult.

The disadvantages are that (1) normal winking is interfered with and (2) lagophthalmos is present in sleep. Neither of these complications is serious. The absence of normal winking is scarcely noticed, especially by the layman. The lagophthalmos during sleep gives the surgeon some concern because of the danger of drying and ulceration of the cornea. I believe that this danger has been overemphasized, for in not one of the present cases has it been a serious problem. Every cornea has gradually adjusted itself to exposure without ulceration or scarring. I believe this is because a careful vigilance was maintained the first few days after operation and because methyl cellulose was used four or five times a day for two or three weeks after operation. Also, many patients learn a modified Bell's phenomenon, which protects the cornea against exposure during sleep. I have observed several cases in which the patient has learned to turn his cornea on the side of the lagophthalmos under the outer canthus when closing his eyes, thus preventing exposure. This is something the patient has learned without conscious effort on his part so far as I know. In only 1 case (case 2) did ulceration of the cornea develop, and this occurred in a boy who had been struck in the eye three days previously with a snowball.

Even though the surgeon cannot attain perfect results in all cases of ptosis, nevertheless, he can generally improve the patient's appearance functionally and cosmetically. No one can create levator muscle tissue where it does not exist. All any surgeon can reasonably hope to accomplish in these trying cases is to utilize the tissues available to the best advantage. With this in mind, I believe the operation described here will fill an urgent need in the surgical treatment of ptosis.

#### REPORT OF CASES

CASE 1.—On Nov. 9, 1945, D. G., aged 2 years, was brought to the ophthalmology department of the Vanderbilt Clinic with a history of ptosis of the right upper lid since birth (fig. 11). Examination showed complete ptosis of the right eye with little or no levator action and with normal extraocular movements.

On November 19, a resection of the levator palpebrae muscle was done on the right eye, with little or no improvement in the ptosis. On April 25, 1947, therefore, the superior rectus muscle was shortened 5 mm. and the upper lid margin raised to 1 mm. below the limbus according to the technic described here. At the first dressing, four days later, the upper lid had fallen 2 mm. and now overlapped the cornea 3 mm. Slight staining of the cornea developed, but disappeared after use of methyl cellulose for twelve hours.

previously described. On the fifth post-operative day the Frost sutures were removed, after which faint staining of each cornea developed. This cleared up promptly in a day or two with the use of methyl cellulose. One month after the operation the patient presented the appearance shown in figure 12. At this time some weakness of each superior rectus could be brought out in the extreme superior temporal fields, but the patient did not complain of diplopia.

Ten months after the operation the child reported to the clinic with an ulcer of the left cornea, stating that a few days before he had been struck in this eye with a piece of snow. The ulcer cleared up in three weeks with the use of liquid petrolatum and a patch, leaving a thin scar adjacent to the pupillary area.

*Comment.*—This case is the only one in this series in which a corneal ulcer with scarring developed after operation from any cause. The

ulcer was definitely caused by the injury and not by exposure; and the ulcer cannot be attributed to the operation, for the patient has always been able to close his eyes voluntarily, with effort.

It should be noted that, even though each superior rectus muscle was normal before operation, no overaction occurred after both muscles were shortened. As a matter of fact, just the reverse effect was present after operation, for slight weakness was detectable in extreme rotation into the field of action of each superior rectus. Therefore, it would seem that resection of the superior rectus muscle is indicated in all cases of complete ptosis in which this muscle is used to support the lid, even when the superior rectus is normal. When the superior rectus is paralyzed or paretic, more muscle tissue (8 to 12 mm.) should be resected.

CASE 3—G. M. C., a youth aged 18, consulted Dr. Gordon M. Bruce on Nov. 18, 1947 because of bilateral ptosis, greater in the right eye, which had been present since birth. Examination showed his vision to be 20/20 in each eye with correction. The ptosis of the right eye measured 3 mm. with eyes down,

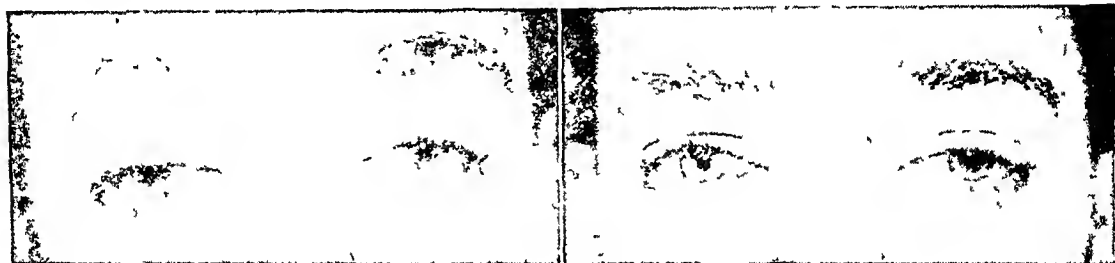


Fig. 13 (case 3)—Bilateral ptosis, greater in the right eye. Note in the picture before operation that both eyebrows are elevated in an attempt to uncover the right pupil. After operation, this muscle action of the frontalis is absent, a good upper lid fold is present and the ptosis is well corrected. The left upper lid will be raised at a later date to correspond to the right.

5 mm. with eyes in the primary position and 3 mm. with eyes up. Action of the levator muscle was absent in the right eye but was good in the left eye. Extraocular motility and the fundi were normal.

On December 16, Dr. Bruce shortened the right superior rectus 6 mm. and carried the muscle tongue forward into the tissues of the upper lid, according to the technic described.

The patient made an uncomplicated recovery, and when he was last seen, on April 2, 1948, his vision was 20/20 with correction in each eye and both eyes were quiet (fig. 13).

CASE 4.—Master J. K., aged 2, was seen by Dr. J. H. Dunnington on May 7, 1948, because of ptosis of the left upper lid since birth. Examination showed bilateral ptosis, greater in the left eye, the fissures with the eyes in the primary position, measuring 7 mm. in the right eye and 4 mm. in the left eye. Extraocular muscle movements seemed normal.

On June 16 the left superior rectus was shortened 8 mm. and, after division of the muscle tongue into three smaller tongues, the latter were carried forward

into the upper lid and tied so that the margin of the upper lid was at the upper portion of the limbus.

The dressing was changed on the fourth day. Faint staining of the cornea was noted the next day but cleared up promptly with the use of methyl cellulose three times a day.

of the levator muscle was attempted but abandoned because no true levator tissue was found. Instead, a Wheeler orbicularis transplantation for ptosis was done. The patient made an uneventful recovery, with improvement of 2 mm. in the ptosis, but definite weakness of the left superior rectus muscle developed after the operation.

On Dec. 1, 1944, one year after the operation, the ptosis measured 2 mm. with eyes directed up, 2 mm. with eyes in the primary position and zero with the eyes looking down (fig. 14). At this time a second operation was done to correct the residual ptosis and the weakness of the superior rectus muscle by



shortening the latter 7 mm. and carrying the tongue of the muscle into the tissues of the upper lid, according to the technic previously described. The cornea was covered by means of a Frost suture. The patient made an uneventful postoperative recovery, and when last seen, on Dec. 27, 1946, two years after the operation, she had no complaints and the ptosis was well corrected. At no time since the operation has the patient complained of ocular discomfort, nor has staining of the cornea been present, even though the left eye is partly open during sleep. Residual weakness of the left superior rectus is still present, especially in looking upward (fig. 14), but diplopia has never been present.

*Comment.*—The weakness of the superior rectus was not demonstrable until after the Wheeler orbicularis operation for ptosis had been done, indicating that suspension of the upper lid from a normal superior rectus tends to weaken the lifting power of this muscle. Therefore it is only reasonable to foresee this induced weakness when utilizing the superior rectus to support the lid and to shorten the muscle at the time of operation, thus increasing its lifting power and preventing or reducing to a minimum postoperative hypotropia and diplopia.

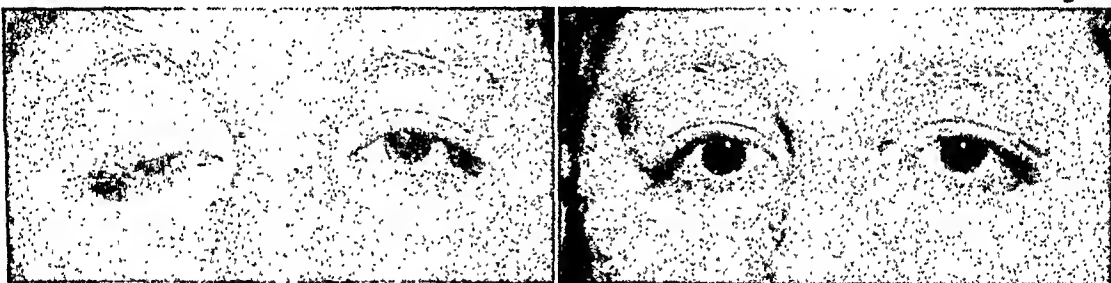


Fig. 15 (case 6).—Complete ptosis of the right upper lid with weakness of the right superior rectus before operation. After operation, the ptosis was well corrected, and a natural-appearing upper lid fold was produced.

CASE 6.—Master J. M., aged 15, came to the Vanderbilt Clinic on Aug. 2, 1945, complaining of ptosis of the right eye, which had been present since birth. He stated that when he was 5 years of age an operation to raise the upper lid had been performed elsewhere. Examination showed his vision to be 20/50 in the right eye and in the left eye, 20/30 + 3 correctable to 20/20 in the right eye and 20/20 + in the left eye. The ptosis of the right eye measured 7.5 mm. with eyes directed up, 5.5 with eyes directed straight ahead and zero with eyes directed down (fig. 15). Examination of the extraocular muscles showed slight weakness of the right superior rectus, moderate weakness of the right inferior rectus and some weakness of the right inferior oblique. An exotropia of 6 to 11  $\Delta$  suggested an incomplete paralysis of the third cranial nerve, but no definite weakness of the right internal rectus was demonstrable. The right external rectus and the right superior oblique muscle seemed normal. Levator action was entirely absent. Measurement of the fields for diplopia showed left hypertropia with eyes directed up and right and with eyes up and left but right hypertropia with eyes directed down and to the right, indicating weakness of the right superior rectus, the right inferior oblique and the right inferior rectus muscle.

On Sept. 18, 1945 a modified Moutais operation was done in which the superior rectus was shortened 6 to 8 mm., according to the technic described. A Frost suture was inserted into the lower lid to cover the cornea for four days. The patient made an uneventful postoperative recovery (fig. 15). At no time since the operation has the cornea stained with fluorescein, nor has the patient complained of diplopia or of irritation, even though his right eye does not close completely during sleep.

*Comment.*—This patient had either a paresis of the third nerve with involvement of the superior rectus, the inferior rectus, the inferior oblique and the levator muscle or an aplasia of the extraocular muscles due to faulty embryonic development. In such a case one cannot hope



Fig. 16 (case 7).—(A) Complete ptosis with weakness of the superior rectus in each eye. (B) After operation the ptosis was well corrected, a normal curve of the upper lid was produced and a natural-appearing upper lid fold was present. No diplopia or staining of cornea has ever been present. (C) Note that the patient can close her eyes after the operation.

to restore normal extraocular motility. All one can reasonably hope to accomplish is to improve the cosmetic appearance in the primary position.

CASE 7.—J. B., a girl aged 4 years, was brought to me because of drooping upper eyelids since birth. In order to see straight ahead, she had to raise her chin to the horizontal plane. She was mentally retarded and had six toes on the right foot (two webbed and two stumps) and two webbed toes on the left foot. No one in the immediate family had ptosis or other anatomic abnormalities. Examination showed no central fixation in either eye, complete ptosis of each upper lid with no levator action, and to and fro mixed nystagmus, esotropia

of 30  $\Delta$  and definite limitation of ocular elevation in each eye. In addition, she had bilateral hyaloid arteries with retrolental fibroplasia and retinal folds.

In October, 1945 each superior rectus was shortened 6 mm. and the resected tongue of the superior rectus muscle carried forward into the upper lid to correct the ptosis, according to the technic described. The patient made an uncomplicated recovery and one year and three months after the operation presented the appearance shown in figure 16. At no time have the eyes watered or become red, even though both eyes remain open during sleep.

When she was last seen, in June 1948, two and one-half years after the operation, both eyes were quiet, the ptosis remained slightly overcorrected and there was still present a slow to and fro nystagmus. Most of the time her eyes were roughly straight, but at times they were crossed. Ocular elevation was improved, but remained limited in each eye.

*Comment.*—The ptosis in this case was intentionally overcorrected at the time of the operation, under the impression that it was necessary to do so in order to get adequate postoperative correction. In later cases the upper lid was not raised beyond the upper portion of the limbus. As a general rule the upper lid does not need to be overcorrected more than 1 or 2 mm. at the time of operation unless it is unusually heavy and thick. Most normal upper lids overlap the upper limbus 2 to 3 mm., so that if the upper lid is placed at the upper limbus at the close of the operation, the lid will "fall" this amount by the time the first dressing is done, four or five days after the operation. This falling of the lid is thought to be due to postoperative edema, stretching of the tongues of the superior rectus muscle, pulling out of the sutures or contraction of the orbicularis muscle.

CASE 8.—Miss M. K., aged 20, came to the Vanderbilt Clinic on Oct. 19, 1945, complaining of ptosis of the right eye, which had been present since birth. She stated that from 1940 to 1944 the right eye had been operated on elsewhere three times for ptosis and exotropia. Examination showed complete ptosis of the right eye, a scar in the right upper lid (probably from a frontalis muscle operation for ptosis) and scar tissue in the conjunctiva over the internal and external rectus muscles. There was complete paralysis of all the extraocular muscles innervated by the third nerve, and the right pupil was fixed and smaller than the left. Vision was 20/30 in the right eye and 20/20—3 in the left eye, and both fundi were normal.

On Nov. 6, 1945 the right inferior rectus was recessed 5 mm., the right superior oblique tenectomized 4 mm., the right superior rectus shortened 5 mm. and the tongue of the superior rectus muscle carried forward into the upper lid, according to the technic described. At the conclusion of the operation the cornea was covered by means of a Frost suture through the lower lid.

The postoperative course was uneventful except for moderate epiphora of the right eye and faint stippled staining of the corneal epithelium with fluorescein for three or four weeks after operation. When she was last seen, on April 25, 1947, seventeen months after the operation, there was no staining of the cornea, and the patient was pleased with her appearance, although the palpebral fissure of the right eye remained 1 mm. narrower than that of the left eye and movement of the right eye was greatly limited in all directions of gaze.

*Comment.*—Patients with complete paralysis of the third nerve present a difficult cosmetic and functional problem, because not only must the ptosis be corrected but the heterotropia must also be remedied. Even after the ocular deviation and the ptosis have been corrected, the patient has little control of the eye because of the multiple extraocular muscle paralyses. Even though this operation for ptosis leaves much to be desired in cases of this condition, it gives a better cosmetic and functional result than any other operation for ptosis I know of.

CASE 9.—On Oct. 18, 1940 Master A. F., aged 9 months, was first brought to the Vanderbilt Clinic because of drooping of the left upper lid since birth. In March 1942, when he was 2 years old, the ptosis measured 7 mm. with eyes directed up, 6 mm. with eyes directed straight ahead and zero with eyes down. The extraocular muscles were normal.

On March 10, 1942 a Young operation for ptosis was done on the left eye, with little or no improvement in the ptosis; so on April 13, 1943 a Motais-Kirby operation was performed. After this the ptosis was greatly improved, but weakness of the left superior rectus developed, which produced right hypertropia of  $40\Delta$  with eyes directed up and to the left. To correct the hypertropia and the 1 mm. of remaining ptosis, the left superior rectus was shortened 5 mm. and the tongue of the superior rectus muscle carried forward into the upper lid on Jan. 10, 1946. Eight days after the operation the patient returned to the clinic with an area of superficial staining of the cornea directly under the left upper lid, which disappeared in a few days with the use of methyl cellulose.

When last seen, in July 1948, two and one-half years after the last operation, the patient was comfortable, and the cosmetic result was good. However, some weakness of the levators of the left eye persisted, producing a right hypertropia of  $14\Delta$  in the primary position.

*Comment.*—In this case, as in case 1, weakness of the superior rectus muscle developed after the Kirby-Motais operation for correction of the ptosis. In another survey<sup>1</sup> on the results of operations for ptosis of this type, it was shown that in 74 per cent of cases postoperative weakness of the superior rectus developed. Therefore it would seem wise to shorten the superior rectus, even when normal, whenever one is doing a Motais operation in order to prevent or to reduce to a minimum postoperative hypotropia and diplopia.

CASE 10.—Miss C. B., aged 9 years, had had complete ptosis of the left eyelid since birth, for which two frontalis muscle operations had been done elsewhere, without improvement. Examination showed vision of 20/20 in the right eye and 20/70 in the left eye, unimproved by glasses. There were complete ptosis of the left eye, two scars in the skin of the left upper lid, some misdirected cilia (presumably from the two previous operations) and left hypertropia of  $10\Delta$  in the primary position, which increased to  $40\Delta$  with eyes directed up and to the left. A diagnosis was made of complete ptosis of the left eye with complete paralysis of the left superior rectus muscle.

In April 1946 the left superior rectus was shortened 8 to 10 mm., the left inferior rectus recessed 5 mm. and the left superior oblique tenectomized 5 mm.

At the same time, the muscle tongue from the superior rectus was carried forward into the upper lid to elevate it to the upper border of the pupil, thus matching the upper lid of the opposite eye.

When the dressing was removed five days later, the sutures in the skin of the upper lid had sloughed out, and some pus was present in the wound. One week later the infection had cleared up. The visual axis of the left eye was then horizontal and parallel with that of the right eye in the primary position. However, upward elevation remained limited in the field of action of the left superior rectus. When the patient was last seen, in September 1946, five months after the operation, the ptosis was well corrected, the weakness of the left superior rectus persisted, but the general appearance was greatly improved. However, the scars in the skin of the upper lid and the misdirected cilia remained.

*Comment.*—Complete ptosis with complete paralysis of the superior rectus is one of the most difficult types of ptosis to correct. No matter what operation is done, a perfect cosmetic and functional result is impossible. The most one can hope for is to correct the ptosis and the hypotropia, so that the cosmetic result will match the fellow eye in the primary position.

CASE 11.—Master G. Y., aged 5 years, came to the Vanderbilt Clinic on Nov. 18, 1946, because of drooping of the left upper lid since birth. Examination showed bilateral ptosis—greater on the left side—associated with esotropia of  $30^\circ$  and severe weakness of the left superior rectus muscle.

On Nov. 21, 1946 the left inferior rectus was recessed 5 mm., the left superior rectus muscle was shortened 8 mm. and the resected tongue from the superior rectus was carried forward into the upper lid to correct the ptosis.

The child made an uneventful postoperative recovery, and when he was last seen, on July 14, 1947, six months after the operation, the cosmetic result from the operation was good. However, a moderate amount of left hypotropia persisted. At no time did the patient have any trouble from exposure of the cornea, even though the patient left for his home, hundreds of miles away, shortly after the operation and was not seen again in the clinic for six months.

*Comment.*—In cases in which the superior rectus is paralyzed or very weak, it is not enough to shorten this muscle. To correct the hypotropia adequately, it is necessary also to recess the inferior rectus at least 5 mm. If this is not done, the ptosis only will be corrected and the hypotropia will remain. If the inferior oblique also is weak, then the relative lifting power of this muscle can be increased by tenectomizing the direct antagonist, the homolateral superior oblique muscle. This is easily accomplished at the time of shortening the superior rectus because the reflected tendon of the superior oblique lies directly under the tendon of the superior rectus muscle.

CASE 12.—Mr. J. R., a chauffeur aged 46, was seen in the ophthalmologic department of the Vanderbilt Clinic on April 18, 1947, with ptosis of the right upper lid. He stated that his ptosis first developed in 1935, three weeks after an injury to the right upper lid. In August 1941 the right levator muscle had been resected, and in November of the same year a Mota's operation had been done. After the last operation diplopia was present in looking straight ahead in the

horizontal plane unless he raised his chin. Examination of his eyes in April 1947 showed vision 20/20 in each eye without correction and marked ptosis of the right upper lid, associated with right hypotropia of  $12\Delta$  in the primary position, which increased to  $35\Delta$  in the field of action of the right superior rectus.

On May 6, 1947 the right superior rectus was shortened 10 mm. and the muscle stump carried forward into the upper lid, so that the margin of the upper lid was level with the upper portion of the limbus at the close of the operation. After removal of the Frost suture on the fifth postoperative day, a small area of staining of the cornea developed within the first twenty-four hours; this soon cleared with use of methyl cellulose. Six weeks after the operation, no diplopia was present with the eyes in the primary position, the cornea did not stain and the ptosis was well corrected except for slight sagging of the lateral third of the upper lid.

*Comment.*—When using this operation for adults, one must guard against lesions of the cornea for weeks after operation, for the corneal epithelium of an adult takes longer to adjust itself to exposure to the air than that of a child. This is to be expected, because the tissues of children are more adaptable than those of adults and because it is unreasonable to expect a corneal epithelium which has been covered by the upper lid for twenty or thirty years to adjust itself within a few days to drying in the air. In some adults it may be necessary to cover the exposed cornea by pulling the lower lid up over the cornea at night by means of a strip of adhesive plaster attached to the cheek and anchored to the skin of the brow. If this regimen is followed at night and methyl cellulose used three or four times in the daytime, the corneal epithelium will adjust itself in a few weeks to the new conditions forced on it.

CASE 13.—R. W., a youth aged 16, consulted Dr. A. B. Reese with exophthalmos of the right eye. A Krönlein operation, done by Dr. Reese, exposed an extensive pseudotumor within the muscle cone, which was adherent to all the retrobulbar tissues and was removed with difficulty. After this operation, the patient's vision improved from 15/200 to 20/40, and a previously existing papilledema of 6 D. completely subsided. However, paralysis of ocular elevation with ptosis developed. An operation was done on June 30, 1947 by Dr. Reese to elevate the globe and to correct the ptosis by shortening the superior rectus muscle 8 mm. and by transplanting and anchoring the resected tongue to the tissues of the upper lid, according to the technic aforescribed. After the operation, considerable edema of the upper lid and a small area of superficial staining of the cornea developed. Both these conditions soon disappeared, and when the patient was last seen, in February 1948, eight months after operation for ptosis, vision in the left eye had improved to 20/25, with correction. The ptosis was improved, but there was little movement of the globe in looking up. Obviously, the nerve supply to the superior rectus and the levator had been injured during the Krönlein operation.

CASE 14.—Miss J. L., aged 35, came to the Vanderbilt Clinic with congenital ptosis of the left eye. Three operations for ptosis had been done on this eye twenty-seven, twenty-five and twenty-one years before, respectively, with slight improvement after each operation. Examination showed 5 mm. of ptosis (fig. 17) of the left upper lid with pronounced left hypotropia of  $45\Delta$  in the primary position, associated with complete paralysis of the left superior rectus. There

remained only 3 mm. of the upper tarsus of the left eye, indicating that she had had one or more resections of the tarsus and/or the levator muscle.

On July 2, 1948 the inferior rectus was recessed 6 mm., the superior rectus shortened 10 mm. and the ptosis corrected by carrying the tongue from the superior rectus into the tissues of the upper lid. At the same time the superior oblique was tenectomized under the superior rectus to increase the relative lifting power of the left inferior oblique. A Frost suture was inserted into the lower lid to cover the cornea, and a pressure dressing was applied. The dressing and the Frost suture were removed on the fourth postoperative day and the eye left uncovered. There was slight staining of the cornea at times for the first three weeks, but when the patient was last seen, on August 6, one month after operation, there was no more staining. The ptosis was well corrected, and the hypotropia was improved (fig. 17).

CASE 15.—Master L. K., aged 1½ years, was seen in the ophthalmology department of the Vanderbilt Clinic on Dec. 14, 1945 because of ptosis of the right eye. A Dickey operation for ptosis with use of preserved fascia lata had been done two and one-half months before. Examination was essentially noncontributory except for complete ptosis of the right eye associated with paralysis of ocular elevation and the jaw-winking phenomenon of Marcus Gunn. The right



Fig. 17 (case 14).—(A) Complete ptosis of the left upper lid with paralysis of the left superior rectus muscle. Three operations for ptosis had been done on this eye, leaving very little tarsus. (B) Note that the ptosis is well corrected and that some hypotropia of the left eye remains. The sagging of the upper lid to either side of center is due, at least in part, to partial absence of the tarsus.

eye showed 30  $\Delta$  of hypotropia in the primary position, and the complete ptosis of the right eye was decreased intermittently about 50 per cent by chewing gum.

On April 14, 1947, with the child under general anesthesia, a traction test on the inferior rectus, made by passing a muscle hook under it and exerting traction forward, showed that the muscle was nonelastic. This muscle was thought to be fibrotic and was therefore recessed 6 mm. At the same time the superior oblique was tenectomized 5 mm. under the superior rectus, the superior rectus was shortened 6 to 8 mm., and the muscle tongue from the latter carried forward into the tissues of the upper lid and tied to bring the upper lid even with the upper portion of the limbus. The cornea was covered by means of a Frost suture in the lower lid.

After removal of the dressing on the fourth day, there was faint superficial staining of the cornea for seven days. This condition was favored by the fixed position of the right eye in looking up or down, which was due to the fibrotic, nonelastic inferior rectus. The ptosis was well corrected; the jaw-winking reflex was cured; the hypotropia was greatly reduced, and the patient could close his right eye voluntarily. One month later, when the child was seen at the clinic, the eyes were white and there was no staining of the cornea or tearing.

On Nov. 11, 1947 the mother stated that the child slept with the right eye open but that there was no discomfort, tearing or staining. On May 9, 1948 the patient came to the clinic with a foreign body embedded in the cornea over the pupillary area. On May 11 the eye was white.

CASE 16.—Master A. K., aged 4, came to the Vanderbilt Clinic with a history of ptosis of the left upper lid since birth. Examination showed incomplete ptosis of the left eye associated with the jaw-winking phenomenon of Marcus Gunn and with definite weakness of the left superior rectus muscle.

On May 27, 1948 the right superior rectus was shortened 8 mm.; the aponeurosis of the levator muscle was excised for a width of 4 to 5 mm. over the anterior surface of the tarsus, and the muscle tongue from the superior rectus was carried forward into the upper lid and tied, so that the upper lid overlapped the cornea about 1 mm. The dressing was removed on the fifth postoperative day, and the patient was discharged on the eighth postoperative day, with instructions to his parents to use methyl cellulose three times a day and at bedtime.

When seen in the clinic two months after the operation, there was residual left hypotropia, a good upper lid fold and no jaw-winking reflex. When the patient looked downward about 20 degrees below the horizontal plane, the cosmetic appearance was excellent; the visual axes of the eyes were parallel, and the upper lids matched well as to position, contour and presence of the upper lid folds.

CASE 17.—Master I. S., aged 7, consulted Dr. A. B. Reese in October 1945 with a history of ptosis of the right upper lid since birth. Examination showed vision of 20/70 in the right eye and 20/15, uncorrected, in the left eye, 4 mm. of ptosis of the right upper lid, paralysis of the right superior rectus and the jaw-winking phenomenon of Marcus Gunn. On November 23, the right superior rectus was shortened 6 mm. by Dr. Reese, and the muscle tongue was carried forward and anchored to the tarsus of the upper lid. The cornea was covered by pulling the lower lid upward by means of a Frost suture.

When the child was last seen, in January 1946, six weeks after the operation, 1 mm. of ptosis remained, but the jaw-winking reflex was cured and the upper lid moved synchronously up and down with the globe.

*Comment.*—At least 75 per cent of patients with the jaw-winking phenomenon of Marcus Gunn have weak superior rectus muscles associated with the ptosis. Cases of this kind present a problem, because not only the ptosis but the jaw-winking phenomenon and the hypotropia must be corrected. These three objectives can be accomplished by the operation described here if, at the same time, the aponeurosis of the levator muscle is excised for 5 to 6 mm. anterior to the tarsus.

CASE 18.—Miss K. C., aged 12, was seen in the Vanderbilt Clinic on Jan. 6, 1947 because of a residual ptosis of the left eye. She stated that she had been born with a drooping left upper lid, which moved up and down when she chewed. In January 1940, when 5 years old, a Wheeler orbicularis operation had been done to correct the ptosis. At the same time a portion of the levator tendon had been excised anterior to the tarsus to destroy the action of the levator and correct the jaw-winking phenomenon. After this, the jaw-winking phenomenon disappeared, but some ptosis remained, so that in July 1942 a partial tarsectomy was done.

Examination in January 1947 showed vision of 20/30 in the right eye and 20/40, uncorrected, in the left eye. The left eye was directed downward and



outward, producing exotropia of  $24\Delta$  and right hypertropia of  $42\Delta$  in the primary position. One or 2 mm. ptosis remained, but the jaw-winking phenomenon was not present.

On January 22, the inferior rectus muscle was recessed 5 mm., the superior rectus was shortened 6 to 8 mm. and the tongue of the superior rectus muscle carried forward into the upper lid to correct the remaining ptosis.

On the fifth day after this operation the upper lid became infected and pus exuded from the wound. The swelling and infection subsided in one week, leaving a scar of the upper lid. Six months after the last operation  $30\Delta$  of left hypotropia was still present, but the ptosis was overcorrected 1 mm. with regard to the upper limbus of the left eye. This overcorrection was attributed to contraction of scar tissue following the infection of the upper lid. (At the conclusion of the operation the upper lid overlapped the upper portion of the limbus 1 to 2 mm.)<sup>9</sup> At no time since the operation has corneal staining developed, despite the fact that the upper lid does not cover the cornea in sleep.

*Comment.*—It is difficult to evaluate the final result in this case because the patient had had two previous operations for ptosis and because the infection in the upper lid following the last operation had an unknown effect on the final result. This patient had been treated for two weeks prior to operation with penicillin ointment because of a sty of the left upper lid, and it may be that some of the organisms were still present at the time of the last operation.

CASE 19.—Miss C. C., aged 15, came to Dr. J. H. Dunnington in July 1948 with complete ptosis of the left eye associated with the jaw-winking phenomenon. Eleven years before, the left superior rectus had been resected, the left inferior oblique advanced and the left levator resected. On examination in July 1948 the left eye was in good position, but the patient was unable to elevate it. Besides, there was almost complete ptosis associated with the jaw-winking phenomenon.

On July 21, 1948 a nonelastic left inferior rectus was recessed 3 mm., the left superior rectus shortened 7 mm. and the ptosis corrected by the method described here. At the close of the operation the upper lid was 2 mm. above the limbus. A Frost suture was inserted into the lower lid and the latter pulled up to cover the cornea. A pressure dressing was applied for four days. When last seen, ten days after the operation, the ptosis was improved and the patient returned to her home in Georgia and has not been seen since.

CASE 20.—R. C., a girl aged 4, came to the ophthalmology department of the Vanderbilt Clinic on June 14, 1946 with bilateral congenital ptosis. There was no history of congenital ptosis in the immediate family, but the father had what the mother described as a "wide nose," simulating that of the patient (fig. 18). Examination showed complete ptosis of both eyes, blepharophimosis of each eye and an abnormally wide space between the inner canthi over the bridge of the nose. Each fissure measured 13 mm. in length, and the distance from one inner canthus to the other was 45 mm. (fig. 18). Both globes and the extraocular movements seemed normal.

9. This is the only case in which the upper lid took a position after operation higher than that at which it had been placed at the time of operation. Usually it is necessary to place the upper lid 1 or 2 mm. above where one hopes to find it when healing is complete.

On August 15, the internal canthal ligaments were advanced 4 to 5 mm. over the bridge of the nose and the external canthal ligaments severed to allow the fissures to be moved nasally. This shortened the distance between the inner canthi from 45 to 38 mm. and lengthened the fissures from 13 to 15 mm.

On October 24, the right fissure was further lengthened by means of an external canthoplasty, the superior rectus shortened 8 mm. and the tongue of the superior rectus muscle carried forward into the tissues of the upper lid according to the technic described here. On Jan. 16, 1947 an exactly similar procedure was done on the left eye. These operations widened and lengthened the fissures several millimeters (fig. 18).

After each of these operations the patient made an uneventful recovery. Faint staining of each cornea was noted for a few days immediately after each of the two last operations; this disappeared with use of liquid petrolatum several times during the day and at bedtime.

*Comment.*—This patient requires another operation to shorten the distance between the inner canthi and to lengthen the fissures, which are so far displaced laterally that it is impossible for her to see simultaneously with both eyes when looking to the right or to the left.



Fig. 18 (case 20).—Complete ptosis with blepharophimosis. Note the great distance between the inner canthi and the S-shaped deformity of the palpebral fissures and lower lids. After operation, the ptosis is less; upper lid folds are present, and the patient can see straight ahead without raising her chin.

At a later date a piece of cartilage will be inserted over the bridge of the nose under the skin to bring the inner canthi toward the midline. This should improve her appearance greatly.

Ptosis of this nature is among the most difficult to correct and requires patience and ingenuity to secure any cosmetic or functional improvement.

#### SUMMARY

More than eighty operations for ptosis have been described, none of which is entirely satisfactory in all cases. Especially difficult are cases in which resection of the levator is contraindicated. In these cases, suspension of the upper lid from the superior rectus by the operation described here is recommended, for several reasons:

1. The superior rectus can be used even though paralyzed.
2. Slipping of the transplanted superior rectus tongue is reduced to a minimum.

3. A smooth upper lid curve results.
4. Entropion, or inturning of the lashes, is prevented.
5. A natural-appearing upper lid fold is produced.
6. Postoperative hypotropia is prevented or reduced.
7. The operation can be done on very young children.
8. The upper lid moves up and down synchronously with the globe.
9. The operation is not difficult.

The only disadvantages of the operation are that normal winking is interfered with and lagophthalmos during sleep occurs. The former is scarcely noticed by the laity, and the latter is no problem because the patient, in some cases, learns to protect his cornea from exposure by turning it to the side under the external canthus when closing his eyes, while in other cases the epithelium of the cornea seems to adapt itself to the exposure.

The operation is modeled more or less after the Motais procedure. It consists in shortening the superior rectus 5 to 10 mm. (depending on the amount of weakness of this muscle) and suturing the resected portion or tongue of this muscle to the tissues of the upper lid.

This operation has been done in 20 cases without failure in any case. In 4 cases in which the superior rectus was normal, no overaction of this muscle was demonstrable after operation, even though the superior rectus was shortened 5 to 6 mm. In 10 cases in which the superior rectus was weak the ptosis and the hypotropia were corrected or reduced. In 5 cases of ptosis associated with the jaw-winking phenomenon both conditions were corrected. In 1 case of ptosis associated with blepharophimosis the ptosis and blepharophimosis were improved.

### CONCLUSIONS

An operation utilizing the superior rectus muscle which is designed to prevent hypotropia and correct ptosis is presented.

The operation has been used in 20 cases without a single failure.

It is recommended only when resection of the levator is contraindicated, for example in cases of (*a*) complete ptosis with a normal superior rectus muscle; (*b*) complete ptosis with a weak superior rectus muscle; (*c*) ptosis associated with the jaw-winking phenomenon of Marcus Gunn, and (*d*) complete ptosis associated with blepharophimosis.

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## OCULAR EFFECTS OF THE CHOLINE ESTERS

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THE OCULAR effects of choline and its derivatives are receiving increased attention not only as important metabolic and physiologic factors but also as therapeutic agents. Until recently use of these compounds in ophthalmology was limited largely to the miotic treatment of glaucoma; however, synthesis by Swan and White<sup>1</sup> of choline esters with mydriatic and cycloplegic properties has greatly increased the possible therapeutic applications of the group. The ocular effects of the first choline to be known have not been fully investigated, nor have the possibilities for synthesis of new and more effective derivatives been fully exhausted; however, there are sufficient experimental data to provide a scientific basis for the clinical application of most of the presently known derivatives. These data are important to ophthalmologists, for, as compared with the commonly used drugs of the alkaloid series, the choline derivatives are unique in their chemical, physical and pharmacologic properties.

Some knowledge of the chemistry of choline is essential to proper application of choline and its esters in ophthalmology. Choline contains a quaternary ammonium group, that is, four methyl groups attached to a nitrogen molecule. In biochemistry and physiology the quaternary ammonium group receives considerable attention as a source of "labile" methyl groups for the metabolism of other substances, but from the ophthalmologic point of view quaternary ammonium groups are important because they dominate the physical properties and thereby influence the corneal penetration and mode of administration of all choline esters. Quaternary ammonium groups have a decided affinity for water; consequently, choline and all of its commonly used esters are extremely hydrophilic (fig. 1).

When a medicament is placed in the conjunctival sac, the distribution of the drug between the drug vehicle and the tissue is generally

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1. Swan, K. C., and White, N. G.: *Proc. Soc. Exper. Biol. & Med.* **53**:164, 1943.

in accordance with the relative affinity of the drug for the vehicle and for the tissues.<sup>2</sup> It is important to apply this "law of relative affinities" to the clinical administration of such highly hydrophilic compounds as choline and its esters (fig. 2). If these drugs are administered in simple aqueous solution, they tend to be retained in the water vehicle, for which they have a high affinity, and little penetrates the corneal epithelium. It is obvious that choline esters would be most effectively administered if suspended in an anhydrous base, such as petrolatum. In these circumstances they have a relatively greater affinity for the

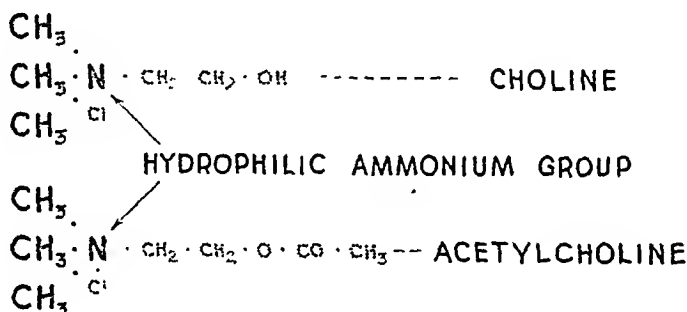


Fig. 1.—Dominant hygroscopic groups in choline and acetylcholine.

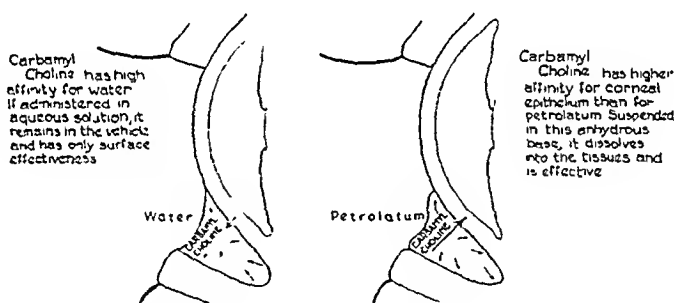


Fig. 2.—Diagram illustrating the law of relative affinities. Distribution of a solute (drug) between two immiscible solvents, e. g., tissue and drug vehicle, is generally in accordance with the relative solubilities (affinities) of the solute in the two solvents.

precorneal film and the epithelium than they do for the vehicle and therefore penetrate the cornea with greater consistency than when instilled in simple aqueous solutions.

The effect of choline chloride on the intraocular muscles is that of a weak stimulation of the sphincter of the iris and the ciliary muscles. These stimulatory effects are greatly increased in certain of its esters. Acetylcholine, the acetic acid ester of choline, is thought to be the chemical mediator of many types of nerve impulses because transmission of

2. Swan, K. C.: Pharmacology and Toxicology of the Cornea, Arch. Ophth. 41:253-275 (March) 1949.

the nerve impulse is associated with release of acetylcholine in the tissues. For example, stimulation of the parasympathetic fibers of the oculomotor nerve results in miosis and cyclotonia due to contraction of the sphincter of the iris and some of the ciliary muscles. This action is associated with release of acetylcholine in these tissues; conversely, acetylcholine injected into the eye simulates stimulation of the parasympathetic nerve fibers. This physiologic action of acetylcholine is terminated by an enzyme, choline esterase, which is present in the tissues, including the iris and the ciliary body. This esterase splits acetylcholine at its ester linkage and rapidly terminates its physiologic action.

Early investigators believed acetylcholine to be inactive on the intraocular muscles because they did not recognize that when instilled in aqueous solution it penetrates the epithelium poorly. Acetylcholine so administered reaches the intraocular tissues at such a slow rate that it is hydrolyzed by the esterase before its pharmacologic effects become manifest; however, even if acetylcholine is effectively administered, e. g., by iontophoresis, its ocular effects are evanescent. For this reason, acetylcholine, while of great physiologic significance, has little direct value as a therapeutic agent. Its greatest importance in ocular therapeutics lies in the enhancement of the physiologic action by drugs which inhibit the choline esterase.

A number of compounds inhibit the choline esterase and thus, by preventing hydrolysis of acetylcholine in the tissues, have an indirect stimulatory action on the iris and ciliary body. One of these drugs, physostigmine, was used clinically as a miotic in the treatment of glaucoma many years before the mechanism of its action was known. The most important component of physostigmine was discovered by Stedman and White<sup>3</sup> to be the urethane group. A number of simple aromatic compounds containing this group have been synthesized, all of which actively inhibit the choline esterase. Neostigmine is the best known example. Another drug with intense and prolonged inhibitory effects on the choline esterase was developed recently from the war gases. Di-isopropyl-fluorophosphate, commonly known as DFP, has the same action on intraocular muscles as physostigmine and neostigmine, but its effects are more intense and prolonged.<sup>4</sup>

Physostigmine, neostigmine, di-isopropyl-fluorophosphate and related compounds which enhance the physiologic action of acetylcholine are spoken of as indirect stimulatory miotics, to distinguish them from drugs like pilocarpine which directly stimulate the sphincter of the iris

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3. Stedman, E., and White, A. C.: *J. Pharmacol. & Exper. Therap.* **41**:259, 1931.

4. Leopold, I. H., and Comroe, J. H., Jr.: Use of Diisopropyl Fluorophosphate ("DFP") in Treatment of Glaucoma, *Arch. Ophth.* **36**:1 (July) 1946.

and from drugs like dibenamine (dibenzyl-beta-choroethylamine) <sup>5</sup> which induce miosis by relaxation of the dilator of the iris. The division of stimulatory miotic drugs into direct and indirect stimulants is of clinical importance, for it largely determines their use in glaucoma (fig. 3).

As might be expected, action of the indirect stimulatory miotics on intraocular muscles simulates the sharp contraction of the iris sphincter and the ciliary muscle resulting from administration of acetylcholine. When the breakdown of acetylcholine is inhibited by these drugs, the sharp contraction is prolonged and is in effect a spasm. The spastic action of physostigmine and related drugs on the intraocular muscles is of particular value in patients with acute congestive glaucoma of the shallow chamber type. In these patients primary concern is to effect a sharp reduction in intraocular tension with a minimum of delay. Vision is so obscured from the acute glaucoma, and the patient is

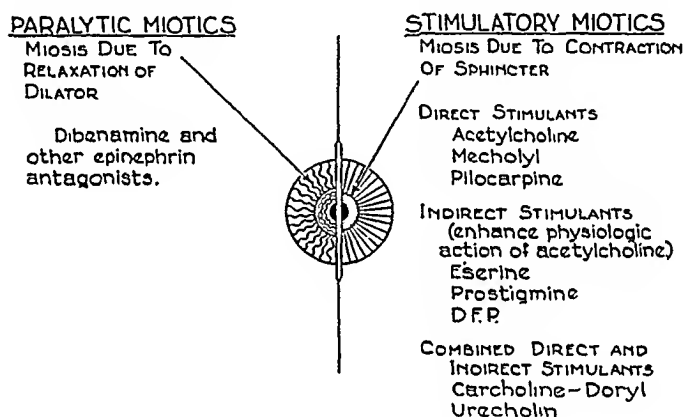


Fig. 3.—Classification of miotics.

already suffering from the pain to such an extent, that the ocular discomfort effected by the drugs is of little consequence. On the other hand, the spastic action of these drugs is a distinct disadvantage in the treatment of patients with chronic noncongestive glaucoma. The violent contraction of the iris sphincter and ciliary muscle is apt to be uncomfortable unless either the drugs are administered in small doses or the maximal effect is maintained by large doses. Also, these drugs have a more profound effect on accommodation than has pilocarpine and thereby disturb vision. In some cases this stimulation of accommodation can be maintained at a fairly constant level and the induced change in refractive error can be corrected by lenses; but in many cases of chronic noncongestive glaucoma this measure is not feasible. In young adults the variation in refractive error due to these medicaments may amount

5. Christensen, L., and Swan, K. C.: Tr. Am. Acad. Ophth., May-June 1949, pp. 489-497.

to several diopters during the day. Also, as the effects of the indirect stimulatory miotics wear off the iris sphincter and the ciliary muscles are hyperreactive and hypertonic. A hyperactive pupillary light reflex may last many days after a single administration of di-isopropyl-fluorophosphate to a normal eye, and a spasm of accommodation may result from only a short period of reading. Moreover, these effects are not limited to the intraocular muscles; e. g., an annoying twitching of the orbicularis may accompany the ocular administration of physostigmine. In contrast, the response of the pupil and the ciliary body will be decreased as the effects of pilocarpine or other direct stimulants wear off. Di-isopropyl-fluorophosphate seems the most effective agent to counteract the effects of atropine, but its use should be reserved for emergency. When it is administered routinely to counteract the effect of mydriatics and cycloplegics, the discomfort that it causes may be greater and more prolonged than the disability of mydriasis and cycloplegia. Di-isopropyl-fluorophosphate seems the drug of choice in the treatment of aphakic glaucoma. In aphakic patients this drug causes little ocular discomfort and no disturbance of vision. The glaucoma can often be controlled by only a few instillations weekly.

It has long been known that in patients who have received physostigmine over a long period not only follicular conjunctivitis but mild anterior uveitis may develop. These inflammations seem to be due to the irritating properties of the free physostigmine base. Addition of an acid buffer to the vehicle prevents the conjunctival reaction but has no influence on the intraocular irritation produced by the drug. It seems that di-isopropyl-fluorophosphate may also produce ocular inflammation. Dunphy<sup>6</sup> has observed cells in the aqueous of patients receiving this drug. In the University of Oregon Medical School Clinics a recurrence of the inflammatory process occurred after administration of di-isopropyl-fluorophosphate in 4 cases of chronic glaucoma developing or persisting after uveitis. In 1 of the cases there had been no active inflammation for eighteen months, and in another case the uveitis had been quiescent for six months. This number of cases is not an adequate basis on which to draw conclusions, but the occurrence indicates that di-isopropyl-fluorophosphate should be used with caution in cases of postinflammatory glaucoma.

When it became apparent that the choline inhibitors were not ideal drugs for the treatment of chronic noncongestive glaucoma, attention of ophthalmic pharmacologists turned to those choline derivatives which had more prolonged pharmacologic effects than acetylcholine. A number of choline esters have been synthesized with greater stability in the tissues than acetylcholine but with the same direct stimulatory effects on

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6. Dunphy, E.: Personal communication to the author.



the intraocular muscles. The onset of their action is more insidious, less spastic and more easily controlled than that of acetylcholine and the previously discussed indirect stimulants. As the effects of these choline esters wear off, the tonus and the reactivity of the iris sphincter and ciliary muscle are reduced, whereas, as previously stated, a hyperreactivity follows use of the indirect stimulants, such as physostigmine and di-isopropyl-fluorophosphate.

Substitution of a methyl group for one of the hydrogen molecules in the beta position increases considerably the stability of acetylcholine in the tissues. This synthetic compound, methacholine chloride U. S. P. (acetyl-beta-methylcholine chloride; mecholyl® chloride), is a highly specific stimulant of parasympathetic structures, including the iris sphincter and ciliary muscles. Methacholine has longer action than acetylcholine but is a short-acting drug. Its maximal effects on the intraocular muscles following instillations into the conjunctival sac last less than an hour. The stimulatory effects of methacholine may wear off completely in several hours and are often followed by a short period of decreased reactivity of the intraocular muscles.

When administered in simple aqueous solution, methacholine, like acetylcholine, penetrates the normal corneal epithelium poorly; consequently, its effects are inconsistent unless precautions are taken to insure its absorption. Disturbance of the corneal epithelium by physical or chemical means greatly increases the penetration of the methacholine. Therefore, a practical method of administering the drug is to precede it with instillation of a topical anesthetic which disturbs the corneal epithelium, for example, 0.5 per cent tetracaine hydrochloride. When this procedure is followed, a single drop of 5 or 10 per cent methacholine chloride consistently produces miosis and cyclotonia; however, the most effective method of rapidly administering the drug is by iontophoresis. Intense miosis with a minimum of systemic effects can often be effected in a matter of minutes.

The action of the methacholine is so short that its use is largely limited to the treatment of acute congestive glaucoma of the shallow chamber type. The administration of methacholine by iontophoresis seems superior to instillations of the drug or of physostigmine. In some patients a drastic drop in tension has been observed to occur within thirty minutes, in contrast to the several hours which are required to bring down the tension when physostigmine is administered by instillation or in an ointment. A patient with acute congestive glaucoma is a true emergency, in which every minute is important in the preservation of vision.

Methacholine, administered by iontophoresis, fills an important need in the treatment of acute glaucoma, but if the apparatus is not available the drug can be administered by instillation. Methacholine solution is

usually well absorbed in eyes with this type of glaucoma, as the corneal epithelium is seldom normal and is further disturbed by the topical anesthesia and trauma associated with instrumental tonometry. Ten per cent methacholine chloride in aqueous solution has not proved more effective than physostigmine in controlling the tension; however, if repeated instillations are required, the patient has a less severe systemic reaction. Physostigmine acts over a period of hours; consequently, its systemic effects become accumulative with successive doses at short intervals. Nausea, diarrhea, pallor, weakness, sweating, salivation and a drop in blood pressure are common signs and symptoms. In contrast, tissue choline esterases terminate the action of methacholine so rapidly that the systemic effects following repeated instillations seldom become summated. This is not to imply that methacholine is not capable of serious systemic reaction. If the drug is administered at too frequent intervals and the epithelial barrier of the conjunctiva and cornea has been reduced by topical anesthesia or trauma, the drug may produce an alarming drop in blood pressure.

Clarke<sup>7</sup> advocated the use of methacholine and neostigmine together for their combined direct and indirect action. This combination is more potent than either of the two drugs used alone; however, in my experience their combined use has seldom been effective when methacholine, administered by iontophoresis, has failed in treatment of acute congestive glaucoma. This result is explained by histologic examination of glaucomatous eyes which have been enucleated because of the failure of therapy. The necrosis of the iris sphincter which occurs in cases of uncontrolled acute glaucoma (fig. 4) suggests that when the muscles are still reactive either of the drugs used alone is sufficiently potent, but when the muscles are severely damaged any combination is ineffective. Also, combination of the two drugs seems to increase their undesirable systemic reactions, notably gastrointestinal disturbances and lowering of the blood pressure.

Carbachol U. S. P. (carbaminoylcholine chloride; carcholin®; doryl®) was synthesized in Germany in 1931. This urethane ester of choline has much greater tissue stability than either acetylcholine or methacholine, its beta methyl derivative. Carbachol has some direct stimulatory action, and its urethane group inhibits the choline esterase; consequently, the drug is both a direct and an indirect stimulatory miotic with prolonged pharmacologic effects. It was first used in 1932 in the treatment of chronic noncongestive glaucoma by Velhagen<sup>8</sup>; but it was not recognized that the compound penetrated the normal cornea poorly when administered in simple aqueous solution.<sup>9</sup> Failure to

7. Clarke, S. T.: *Am. J. Ophth.* **22**:249, 1939.

8. Velhagen, K., Jr.: *Klin. Monatsbl. f. Augenh.* **92**:472, 1934.

9. Swan, K. C.: *Journal-Lancet* **57**:79, 1942.

recognize this fact led to a confusion of reports on the duration and intensity of action of the drug on the intraocular muscles; consequently, its use did not become widespread.



Fig. 4.—Necrosis of the sphincter of the iris of an eye with acute glaucoma (above) and the normal sphincter of an unaffected eye (below).

In 1940 Swan,<sup>9</sup> taking precautions to insure consistent absorption, found that the action of carbachol in cases of chronic noncongestive glaucoma was more intense and prolonged than that of equal doses of pilocarpine. With the use of carbachol in treatment of glaucoma, Swan

and O'Brien<sup>10</sup> introduced the use of highly surface-active (wetting) agents to increase corneal penetration of drugs. Although the value of these agents to enhance absorption of all types of ophthalmic drugs has since been confirmed by other authors, the administration of carbachol in a simple anhydrous ointment base now seems simpler and more effective than wetting agents as a means of administering this agent.<sup>11</sup> Carbachol, like other choline esters, has a high affinity for water; consequently, when administered in aqueous solution carbachol has a much higher affinity for the vehicle than for the corneal epithelium, and little enters the normal cornea. When administered as a dry suspension in pure petrolatum or other anhydrous base, the drug has a greater affinity for the epithelium and precorneal film than for the vehicle and therefore effectively penetrates the cornea (fig. 2). Immediate obscuration of vision by the ointment provides the patient with the assurance that the drug has definitely come into contact with the cornea. Gentle massage of the cornea through the lids further insures absorption.

Carbachol has its greatest usefulness in treatment of chronic non-congestive glaucoma. In this type of glaucoma the compound has advantages over physostigmine, neostigmine and related derivatives in that it does not produce twitching of the eyelids and has a smoother and generally more prolonged action. Although carbachol is a powerful cyclotonic drug, the refractive error may be maintained fairly constant by a regular dosage schedule.

The urethane of beta-methyl choline chloride (carbaminoyl-beta-methylcholine chloride; urecholine<sup>®</sup>) combines the two components which make methacholine and carbachol more stable in the tissues than acetylcholine. The carbaminoylcholine group increases tissue stability by inhibiting the choline esterase, and the beta methyl group increases the stability of the ester linkage. This compound, therefore, is the most potent and the longest-acting of the miotic choline series. Its use in ophthalmology has been limited, but experience with a few patients indicates that it may be more effective than carbachol in the treatment of chronic noncongestive glaucoma. Like carbachol, it penetrates the cornea poorly, and therefore the same precautions are required to insure its absorption.

In their ocular effects and therapeutic uses, carbachol and its beta methyl derivatives are more closely comparable to pilocarpine than to other ophthalmic drugs. When precautions are taken to insure their absorption, these choline esters are more effective and need be admin-

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10. Swan, K. C., and O'Brien, C. S.: Carbaminoylcholine Chloride in Treatment of Glaucoma Simplex, *Arch. Ophth.* 27:253 (Feb.) 1942.

11. Swan, K. C.: Carbaminoylcholine Chloride in Petrolatum, *Arch. Ophth.* 30:591 (Nov.) 1943.

istered less frequently than pilocarpine; however, it is the custom in the University of Oregon to reserve their use for patients who are sensitive to pilocarpine or in whom pilocarpine does not effectively control the glaucoma. Pilocarpine salts are cheap, and for the average case of chronic noncongestive glaucoma they can be effectively administered in simple aqueous solutions. Carbachol, on the other hand, requires special vehicles and a patient sufficiently intelligent and cooperative to take the precautions necessary for its absorption. When these precautions are taken, carbachol fills an important need for patients who have advanced glaucoma. It is often effective in eyes in which operations for glaucoma have been only partially successful.

Carbachol and urecholine® are drugs with potent effects on the autonomic nervous system and therefore are capable of producing dangerous systemic reactions when excessive doses are administered to the eye, or even when the usual dose is given if the epithelial barrier of the conjunctiva and cornea is reduced. For example, the drugs should be administered with caution if topical anesthesia has been administered and the corneal epithelium has been traumatized by instrumental tonometry. In these circumstances corneal and conjunctival penetration of carbachol is tremendously increased, and enough systemic absorption of the drug may occur to effect a decided drop in blood pressure and other symptoms due to generalized parasympathetic stimulation. The drug should be used with caution in cases of asthma, because enough systemic absorption may occur to induce a spasm of the hyper-reactive bronchial muscles and precipitate an asthmatic attack. When these factors are taken into consideration, carbachol and urecholine® are safe drugs to use in treatment of chronic noncongestive glaucoma.

The most characteristic action of the aforementioned choline esters is stimulation of structures innervated by the parasympathetic nervous system, that is, miosis and spasm of accommodation. In the preparation of these compounds, emphasis was placed on the development of more stable and potent derivatives of acetylcholine. The possibility of reversing its characteristic stimulatory action did not receive consideration. Moreover, no attempts had been made to correlate the pharmacologic action and the physical properties of the choline esters prior to the investigation by Swan and White, beginning in 1939. They had observed that the choline esters as a group penetrated the corneal epithelium poorly and that this impenetrability seemed related to the hydrophilic characteristic of the molecule.<sup>12</sup> Also, they noted that all choline esters with miotic action had little influence on the surface tension of water, i. e., these compounds were surface inactive. With this evidence of the profound influence of physical properties on the ocular effects

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12. Swan, K. C., and White, N. C.: *Am. J. Ophth.* 25:1043, 1942.

of the choline esters, Swan and White set out to synthesize and study the ocular effects of choline esters with different physical properties.

A review of the literature revealed no simple choline esters in which the highly hydrophilic quaternary ammonium group had been counteracted or balanced by addition of a large hydrophobic group to the molecule. Investigation of this possibility necessitated synthesis of a new compound in which the highly water-soluble choline group was

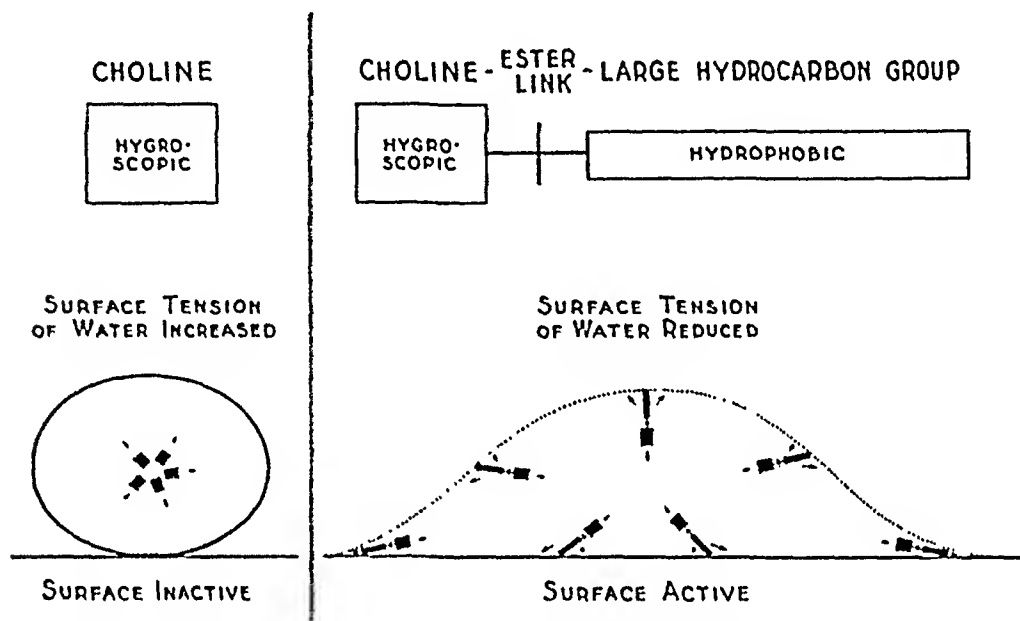
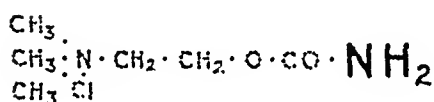
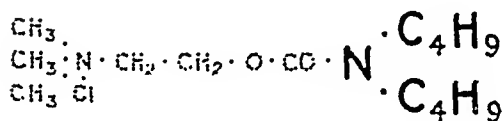


Fig. 5.—Structure and mode of action of surface-active choline esters.



CARBAMYLCHOLINE



DI-*n*-BUTYL  
CARBAMYLCHOLINE

Fig. 6.—Replacement of hydrophilic  $\text{NH}_2$  group in carbachol U. S. P. (carbaminoylcholine chloride) by a water-soluble group, dibutylamine, to form di-*n*-butyl-carbaminoylcholine.

combined through an ester linkage with a large water-insoluble hydrocarbon group. The resultant elongated molecules would be expected to orient themselves at the surface of aqueous solutions and thereby lower surface tension (fig. 5).

Carbachol (carbaminoylcholine chloride), most potent and stable of previously known simple choline esters, was selected for the initial conversion to a surface-active compound. The hydrophilic  $\text{NH}_2$  group was replaced by a water-insoluble group, dibutylamine (fig. 6). The

resultant surface-active compound, di-n-butyl-carbaminoylcholine chloride, was found to have ocular effects the reverse of those of carbachol. Whereas carbachol produced miosis and spasm of accommodation, the new drug produced mydriasis and cycloplegia.<sup>13</sup>

A large number of compounds of this series were synthesized.<sup>14</sup> The mydriatic and cycloplegic actions of these choline esters seem associated with a relatively high surface activity, whereas the choline esters which have little influence on surface tension retain miotic and cyclotonic effects on the eyes. Compounds of intermediate surface activity have little pharmacologic effect.

Dibutoline sulfate (dibutylcarbamate of dimethylethyl-2-hydroxyethyl ammonium sulfate) is the most effective of the new compounds (fig. 7). It induces mydriasis by inhibition of the iris sphincter and recession of the near point of accommodation due to paresis of accommodation. The smooth muscles of the lids and the dilators of the iris, innervated by the sympathetic nervous system, are unaffected. The

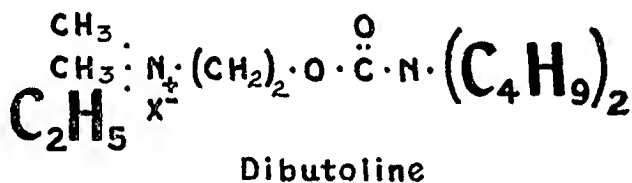


Fig. 7.—Chemical formula of dibutoline.

intraocular effects of dibutoline, therefore, simulate paralysis of the oculomotor nerve and are the reverse of those of acetylcholine.

The action of dibutoline and of di-n-butylcarbaminoylcholine sulfate seems to be peripheral, but the exact nature of the action has not been fully established. The most plausible theory is that the new drugs act as "inhibitory analogues" of acetylcholine. An "inhibitory analogue" is a compound which, by virtue of its chemical similarity to a normal metabolite, replaces the latter in the tissues but is incapable of fulfilling its metabolic functions; consequently, physiologic functions dependent on the presence of the normal metabolite are interrupted. There are numerous examples in bacterial metabolism, notably paraaminobenzoic acid and paraaminobenzenesulfonamide (sulfanilamide). The latter is thought to inhibit the multiplication of certain bacteria by competing with the normal metabolite, paraaminobenzoic acid, for enzymes essential for growth. A similar relation may exist between the new series of choline-like esters and acetylcholine. Acetylcholine normally is involved in the mediation of nerve impulses to tissues like

13. Swan, K. C., and White, N. C.: Di-n-butylcarbaminoylcholine Sulfate: New Cycloplegic and Mydriatic Drug, *Arch. Ophth.* **31**:289 (April) 1944.

14. Swan, K. C., and White, N. C.: *Am. J. Ophth.* **27**:933, 1944.

the iris sphincter and the ciliary muscle. The new compounds are chemically similar to acetylcholine, but they are surface active and would be expected to have greater affinity for the tissues. If the new drugs displaced acetylcholine from the muscle receptor system but were incapable of fulfilling their role in the normal transmission of nerve impulses, relaxation of the involved muscle would result.

The ocular effects of the dibutoline, alone and in combination with other drugs, have now been studied on over 1,000 patients. The initial reports were made with carefully controlled doses on a rather limited number of cooperative patients, and it was assumed that the compound penetrated the cornea readily because of its high surface activity.<sup>15</sup> Later studies have shown that this assumption was not justified; moreover, a few patients seem refractory to dibutoline. The ocular effects and clinical applicability of dibutoline must, therefore, be reevaluated.

Taylor<sup>16</sup> developed a quantitative method for the analysis of dibutoline in the tissue that has made possible accurate determinations of the rate of penetration of dibutoline into the eye. These quantitative chemical studies indicate that the dibutoline, despite its high surface activity, penetrates the normal cornea rather slowly. It penetrates the corneal epithelium but, like other highly surface-active compounds, seems to be retained in this layer. Also, because of its high affinity for water, a good part of the drug tends to remain in the conjunctival secretions and is washed away with the tears.

Extensive clinical experiments have confirmed these laboratory observations that dibutoline, like other choline esters, may be quite inconsistent in its action unless precautions are taken to insure its corneal penetrability. Unfortunately, the "law of relative affinities" cannot be applied to dibutoline. Unlike carbachol and acetylcholine, dibutoline cannot be administered to the cornea in an anhydrous base because it produces injury when concentrated in the epithelium. The epithelial injury that occurs in these circumstances is characteristic of that produced by all highly surface-active agents.<sup>17</sup>

Despite the relative inconsistency of corneal penetration, dibutoline has properties which give it a definite place in ophthalmic therapeutics. In the intensity of its ocular effects the new compound is comparable to homatropine. In most patients it is as effective a cycloplegic as homatropine but is a weaker mydriatic. With homatropine, the busy ophthalmologist cannot depend on pupillary size and reaction to determine whether adequate cycloplegia exists, because the mydriasis is far more intense and prolonged than the cycloplegia. In contrast, dibuto-

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15. Swan, K. C., and White, N. C.: Dibutoline Sulfate: New Mydriatic and Cycloplegic Drug, *Arch. Ophth.* **33**:16 (Jan.) 1945.

16. Taylor, J.: To be published.

17. Swan, K. C.: *Am. J. Ophth.* **27**:1118, 1944.



line has nearly equal effects on the iris and the ciliary muscles; consequently, size and reactivity of the pupil provide a reliable and convenient indication as to the state of cycloplegia. The ocular effects of dibutoline are considerably less prolonged than those of homatropine. Effects of a maximal dose of the drug wear off completely within sixteen to twenty-four hours in the average adult. Dibutoline also differs from homatropine in that undesirable systemic symptoms do not follow its ocular administration in children.

Dibutoline is of greatest value in cycloplegic refraction and internal examination of patients from 35 to 50 years of age. In this age group it produces satisfactory cycloplegia, with a shorter period of visual disability, and there is less danger of precipitating glaucoma than when homatropine is used. The most effective means of administering dibutoline in adults is to precede it with a drop of a local anesthetic to disturb the epithelial barrier. For example, it is the custom in the University of Oregon Medical School Clinics to determine intraocular tension of all adults prior to dilation of the pupils for internal examination. A drop of 0.5 per cent tetracaine hydrochloride is instilled, and the tonometric measurement is made; then two instillations of 5 per cent dibutoline sulfate are effectively absorbed in almost all adults.

The cycloplegic action of dibutoline, like that of homatropine, is too weak to permit use of the drug alone for refraction in children, but in combination with scopolamine dibutoline is valuable because it has low toxicity and a short duration of action. The drug does not produce the circulatory disturbance and excitation and depression of the nervous system which characterize the toxic effects of atropine, homatropine and other drugs of that series. It is my practice to administer to small children a single instillation of 0.2 per cent scopolamine hydrobromide. This dose generally effects a partial cycloplegia and is usually the largest dose which can be administered to small children without evidences of systemic toxicity, such as drying of the secretions and flushing of the face. Rather than wait until the systemic effects of scopolamine wear off before another dose is administered, the cycloplegia is completed with several instillations of 5 per cent dibutoline sulfate. Serious systemic disturbances do not occur, even in infants, and satisfactory mydriasis and cycloplegia often can be obtained in a few hours.

Dibutoline, because of its surface activity, has antiseptic and detergent properties; therefore, it is a valuable drug to be used in cases of laceration of the cornea or infective keratitis, not only to reduce irritation of the iris and ciliary processes but to cleanse the conjunctival sac and to control infection. For this purpose dibutoline is more ideal than any of the previously known compounds. Finally, it may be necessary to use dibutoline as a substitute for drugs of the atropine series in patients

who are allergic to the latter. Dibutoline is chemically unrelated to this group of drugs, and as yet no allergic reactions have been observed. The action of the drug is not sufficiently prolonged for routine use in the treatment of uveitis. For this purpose, scopolamine is more nearly ideal.

#### COMMENT

In this presentation of the ocular effects of some choline derivatives, emphasis is placed on the action of these drugs on the intraocular muscles. These effects are readily subject to careful laboratory study, and a considerable body of data has been obtained. In clinical studies the action of drugs on glaucoma is also subject to careful analysis. As a result, the influence of these drugs on the intraocular tension is fairly well established. There are other ocular effects of these compounds which remain to be investigated, and which may lead to the development of new and more effective therapeutic agents. For example, the choline esters, which are miotics, and the drugs which enhance the physiologic action of acetylcholine are among the most effective agents in the control of glaucoma, but relatively little is known about their effects on the intraocular vascular system and the secretory mechanism of the ciliary body. Only a limited amount of work has been done on the action of these compounds in the biochemistry of the intraocular fluids. It is known that the constituents of these fluids are altered by such drugs as methacholine and that the penetration of various compounds from the blood into the intraocular fluid is influenced.<sup>18</sup> The full physiologic and clinical significance of these facts remains to be established.

The possibility of synthesis of new choline esters of pharmacologic importance has not been exhausted; e. g., no systematic efforts have been made to synthesize derivatives of miotic choline esters with more consistent corneal penetrability. If the hydrophilic properties of the choline derivatives could be reduced without modification of their pharmacologic effects, the value of these compounds in clinical ophthalmology would be greatly increased. Finally, the possibility of synthesis of new mydriatic and cycloplegic drugs of the class discovered by Swan and White has not been extensively investigated. It is quite possible that more effective compounds of this series can be developed. Certainly, none of the currently available mydriatic and cycloplegic drugs are ideal for routine cycloplegic refraction and internal examination of the eye.

#### SUMMARY AND CONCLUSIONS

A decade of laboratory and clinical experiences with the ocular effects of choline derivatives is reviewed. As yet, it is not possible fully to evaluate the influence of these drugs on the intraocular vascular

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18. Swan, K. C., and Hart, W.: *Am. J. Ophth.* **23**:1311, 1940.

system or on the metabolism of the intraocular tissues, but their effects on the muscles of the iris and ciliary body and on intraocular tension seem fairly well established.

The choline esters are hydrophilic and when instilled into the conjunctival sac in simple aqueous solution tend to be retained in the water of the vehicle. In accordance with the "law of relative affinity," choline esters, such as carbachol (carbaminoylethylcholine chloride), are most effectively administered when suspended in an anhydrous base. When so administered, the drug has a relatively higher affinity for the tissue than for the anhydrous base, and corneal penetration is fairly consistent.

The epithelium, with its lipoprotein constituents, is the main barrier to the penetration of the choline esters. Disturbance of this barrier by physical or chemical means may increase the corneal penetration of certain choline esters a hundred fold. The ocular effects may be greatly enhanced, but dangerous systemic reactions may occur.

Acetylcholine is associated with the transmission of stimulatory nerve impulses to the sphincter of the iris and to muscles of accommodation, but its action is so evanescent and its absorption so inconsistent that it has little practical use in ophthalmic therapeutics. The physiologic effects of acetylcholine can be greatly enhanced and prolonged by drugs, such as physostigmine, neostigmine and di-isopropyl fluorophosphate, which inhibit the choline esterase. These indirectly acting stimulants effect a sharp, relatively spastic contraction of the intraocular muscles and increase the tonus of the orbicularis muscle. As their effects wear off, these muscles become hyperreactive. The drastic and inconsistent changes in accommodation, the spastic action of the pupil and the hyperreactivity of the orbicularis muscle which these drugs cause, largely limit their use to the treatment of acute congestive glaucoma. Di-isopropyl fluorophosphate (DFP) seems particularly effective in cases of aphakic glaucoma, but until further studies are made it should be used with caution in cases of postinflammatory glaucoma.

Methacholine chloride (acetyl-beta-methylcholine chloride; mecholyl® chloride) has more prolonged direct stimulatory effects than those of acetylcholine but must still be classified as a short-acting miotic. It is an important drug in the treatment of acute congestive glaucoma of the shallow chamber type. In this condition it has an advantage over drugs like physostigmine in that the systemic effects are not accumulative. Extreme miosis can often be obtained in a matter of minutes when the drug is administered to the cornea by iontophoresis. A rapid drop in tension follows.

Carbachol U. S. P. (carbaminoylethylcholine chloride; carcholin®; doryl®) and the urethane of beta-methylcholine chloride (carbaminoylethyl-beta-methylcholine; urecholine®) are choline esters with prolonged stimula-

tory action on the intraocular muscles. Their hypotensive action in cases of chronic noncongestive glaucoma is more intense and prolonged than that of pilocarpine. They are often effective when pilocarpine fails to control the tension; however, precautions must be taken to insure corneal penetration of these drugs. Special vehicles and massage of the cornea through the lids are required, and the patient must be intelligent and cooperative. In accordance with the "law of relative affinities," these drugs are most effectively administered as a suspension in an anhydrous ointment base.

The pharmacologic action of the choline esters seems related to their surface activity. The miotic and cyclotonic drugs are all relatively surface inactive, whereas the highly surface-active esters of choline seem to have mydriatic and cycloplegic properties. My colleagues and I have synthesized a large number of these compounds, but the possibilities have not been exhausted. Dibutoline seems the most effective of the new class of drugs. It seems to act as an inhibitory analogue of acetylcholine and therefore effects paresis of the sphincter of the iris and the ciliary muscles without affecting the dilator of the iris or the smooth muscles of the lids.

Dibutoline, in the intensity of its mydriatic and cycloplegic action, is comparable to homatropine, but it is less consistently absorbed into the cornea and some patients are refractory to its action. When preceded by instillation of a topical anesthetic, dibutoline is more consistently absorbed and is sufficiently potent to be used as a routine cycloplegic in older adults. It has the advantage that the visual disability which it causes is not so prolonged as that of homatropine, and the size and reactivity of the pupil provide a convenient indication of the degree of cycloplegia. The drug has low systemic toxicity; therefore, it is useful as an adjunct to scopolamine or atropine to produce cycloplegia in children.

In the management of corneal inflammations, dibutoline is valuable because it has detergent and antiseptic action and its mydriatic and cycloplegic effects are not unduly prolonged. Dibutoline is not ideal for the routine treatment of uveitis but fills an important need when the patient is allergic to the atropine series of drugs.

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## SURGICAL TREATMENT OF RECURRENT PTERYGIUM

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PRIOR to World War II recurrent pterygium had been a matter of little concern to most ophthalmologists in the United States. The few patients with primary pterygium who consulted the individual surgeon were handled with satisfaction to both the patient and the physician. Many ophthalmologists had seen no procedure other than McReynolds' transplantation or one of its minor modifications. They were for the most part unaware of the number of papers describing other technics, designed to avoid recurrence, written by men in sections where pterygium is common. The need of this knowledge did not exist for most ophthalmologists in this country. Recurrences were so rarely encountered that one did not inquire into the surgical treatment.

There is a vast difference between an operation for primary pterygium and the surgical management of recurrent pterygium. The first operation is simple and is attended with such a high degree of success that it serves well to introduce the beginner to the field of ophthalmic surgery. On the other hand, the many published technics which have been developed to eradicate the small percentage of recurrent pterygiums attests to the difficulties which beset even the experienced ophthalmologist in dealing with them.

When several patients were admitted to Valley Forge General Hospital in early 1944 with histories of having had from two to twelve previous operations for pterygium, each operation being followed by a recurrence of greater severity, the personnel of the ophthalmology section was unaware of the difficulties associated with this problem. Since practically all forms of treatment had already been tried without avail, it was evident that a different technic must be developed to meet this situation.

As shown in figure 1, the recurrent lesions were thick and extensive. Several patients had symblepharon, ptosis and limitation of motility

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This article is a condensation of a thesis accepted by the Committee on Theses of the American Ophthalmological Society in partial fulfilment of the requirements for membership. The bibliography is given in full, but all case reports and the sections on incidence, etiology, pathology, history of surgical treatment, complications, effect on refraction and animal experiments have been omitted, for the sake of brevity.

severe enough to produce diplopia. It was obvious that in all these patients extensive excision of scar tissue was necessary as a first step in any surgical treatment.

In 1942, at the Institute of Ophthalmology in New York, I had been privileged to remove a highly vascularized intraepithelial epithelioma in an elderly patient; the growth covered the entire cornea and extended about 6 mm. beyond the limbus in all quadrants of the eye. The operative procedure consisted in complete superficial keratectomy and excision of 8 mm. of involved conjunctiva and the episcleral tissue around the entire circumference of the cornea. It was impossible to mobilize enough conjunctiva to cover the exposed sclera. Mucous membrane or skin grafts were avoided, as they would render recog-

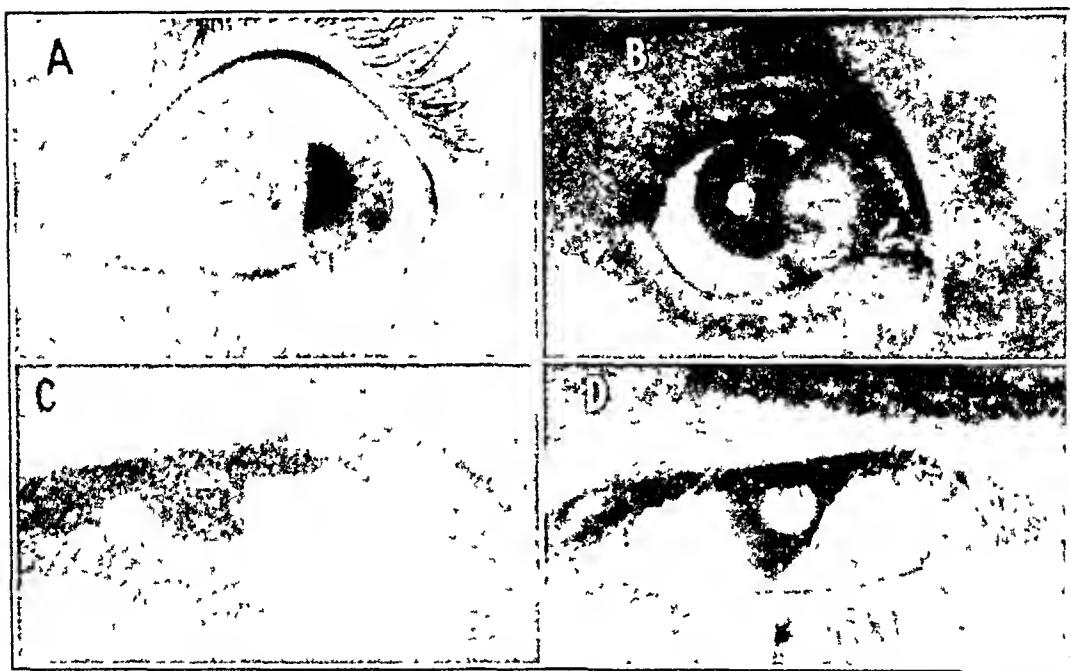


Fig. 1.—Four pictures showing the various types of recurrent pterygia discussed in this paper.

nition of recurrent tumor tissue difficult. The free borders of the conjunctiva and Tenon's capsule were sutured to the outer layers of the sclera at a distance of 7 mm. from the limbus. The large area was left without conjunctival covering with the hope that it would epithelize. Healing was kindly, and there was no staining with fluorescein after ten days. This was a happy result for so radical a procedure, and one which would at first seem to be contrary to accepted surgical principles. Dr. George Wise, of New York, who reported on this case in 1943, states that the tumor has not recurred, nor has there been any vascularization of the cornea during the past six years.

It seemed possible that this technic might be modified for use in preventing recurrence and vascularization of the cornea after complete excision of the recurrent scar tissue in cases of pterygium.

The first patient had had four operations, the last being a transplantation of oral mucous membrane to cover a large defect left after excision of recurrent pterygiums. The photograph (fig. 2 *A*) shows the appearance of the eye. The unsightly graft extended 5 mm. onto the cornea and was elevated about 3.5 mm. It was productive of foreign body sensation and caused pronounced astigmatism. The patient had diplopia on lateral gaze. Since in all previous operations the conjunctiva or mucous membrane had been sutured at the limbus, it was felt that excision of the graft and of all scar tissue, if combined with recession of the conjunctiva, might prevent recurrence and eliminate the restricted mobility of the eyeball. Through the cooperation of Dr. James N. Greear Jr., then Lieutenant Colonel (M. C.), chief of the Eye Section at Valley Forge General Hospital, it was decided to try this technic, and he performed the first operation. The operation was successful and there has been no recurrence in the three and one-half years since operation. The cosmetic result was excellent, as shown in figure 2 *B*. The pronounced corneal astigmatism was largely elimi-

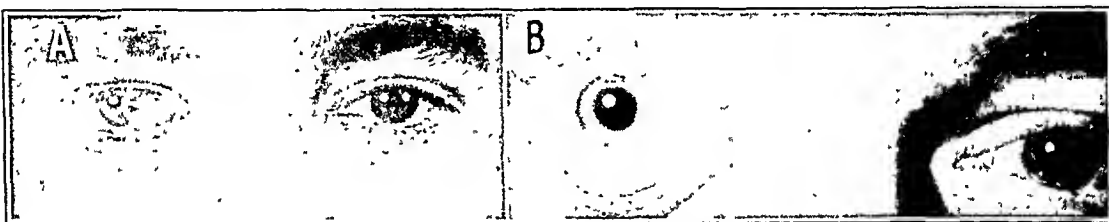


Fig. 2.—*A*, preoperative appearance of mucous membrane graft applied in fourth operation; *B*, postoperative appearance. The gray area is not elevated.

nated. Only a few blood vessels extended onto the cornea, and these were visible only with the slit lamp.

Encouraged by this result, operations were done on other soldiers, with equally good results. In the thesis of which this paper is a condensation, 29 operations, performed on 22 patients, are reported.<sup>1</sup>

The principles of the operative technic to be described have also been applied to pseudopterygiums, to excision of epibulbar tumors, to the correction of symblepharon and to the removal of superficially vascularized corneal scars.

#### OPERATIVE PROCEDURE AND RESULTS

*Operative Technic.*—A superficial lamellar keratectomy is done. The incision is started with a Graefe or a Lunsgaard knife 0.5 to 1 mm. central to the advancing border of the recurrent vascularized connective tissue and is carried back to the

1. Since the thesis was completed, operation has been successfully performed on 9 additional patients at the Valley Forge General Hospital. Two other patients had recurrences, as a result of faulty technic.

limbus in one plane as deep as necessary in order to include all scar tissue. A black silk traction suture placed through the head of the pterygium is useful during the keratectomy for fixation and retraction. Any shreds of connective tissue are carefully removed with the knife or a sharp curet. The dissection is carried beyond the limbus with a Lunsgaard knife, or sharp dissecting scissors if desired. When the dissection is completed to the point where the bulbar conjunctiva is no longer tightly adherent to scar tissue, Stevens scissors are used to undermine the healthy conjunctiva back to the semilunar fold and for about 8 mm. superior and inferior to the borders of the offending scar tissue (figs. 3 to 7).

In some instances the recurrence is made up purely of scar tissue; in others there are what appear to be portions of the original tissue of the pterygium. The amount of conjunctiva adherent to this tissue varies a great deal. It is advisable to save as much healthy conjunctiva as possible as one excises all the recurrent scar tissue. Therefore submucous excision, as advocated by several surgeons, can be done to advantage. It should be noted that one is attempting to recess, rather than to excise, conjunctiva. However, it is necessary to excise all the scar tissue and abnormally adherent conjunctiva over it, as this subcon-

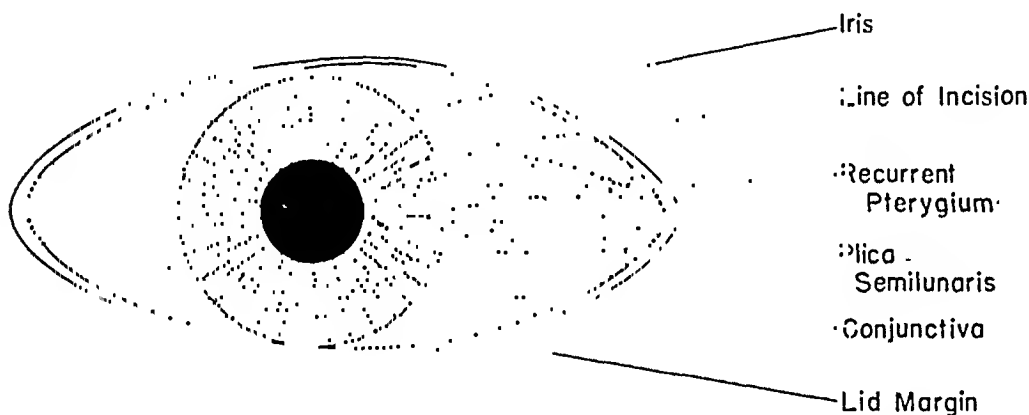


Fig. 3.—Preoperative appearance and lines of incision. In this diagram and in figures 4 to 7 the scheme for designating tissues is as follows: intact epithelium, dotted areas; ocular muscle tendons, horizontally hatched areas; episcleral scar tissue, obliquely hatched areas, and bare sclera, clear areas.

junctival tissue gives rise to recurrence of the lesion if left in place. Whatever conjunctiva can be saved is recessed to serve as lining for the superior, nasal and inferior fornices, which have often been obliterated to some extent by previous operations. This prevents or corrects symblepharon with the limitation of motion and ptosis which are present in such cases. Sutures on rubber pegs can be passed from the fornices through the lid and tied on the skin surfaces to hold the conjunctiva in place in the fornix, in cases of extensive symblepharon, as advocated by Berens.

After the excision of the scar tissue forming the body of the recurrent pterygium is completed, one often finds still denser connective tissue adherent to the sclera. In 6 cases this scar tissue extended from the nasal border of the tendon of the superior rectus to the nasal border of the tendon of the inferior rectus and outward beyond the insertions of these tendons. This tissue is also excised by sharp dissection, a procedure which is unavoidably tedious and time consuming. It is particularly necessary to excise that portion lying at or near the limbus, and this is just the area where such dissection is troublesome, because



of previous operations and because the sclera is rather thin over the intercalary zone. If a Graefe knife is used for the keratectomy, there is likelihood that one of the incisions may be unduly deep because of the difference in consistency of corneal stroma and the recurrent scar tissue. After such a deep cut has been made, it is difficult to complete the dissection cleanly peripheral to the cut and beyond the limbus. In 2 cases the remnant of connective tissue at this site gave

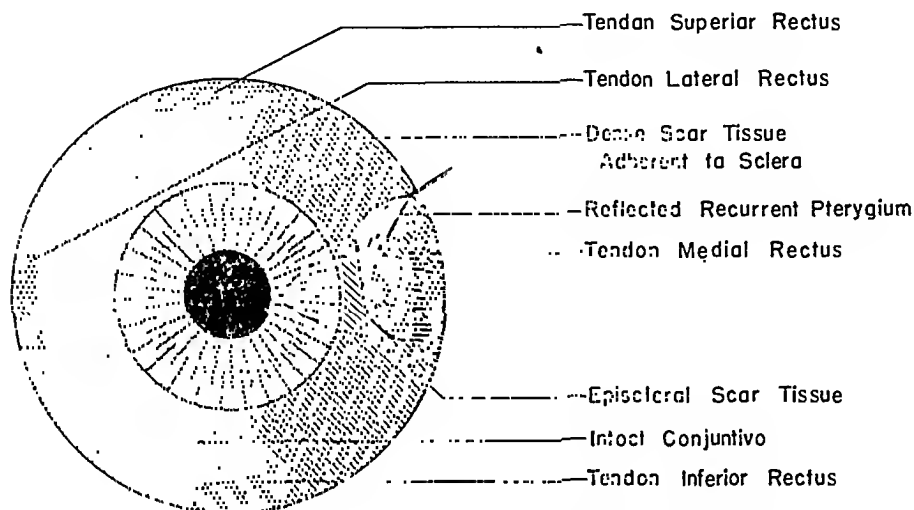


Fig. 4.—Extent of peculiar dense scar tissue tightly adherent to the sclera. It is found only when the conjunctiva is undermined and reflected. It is excised by sharp dissection.

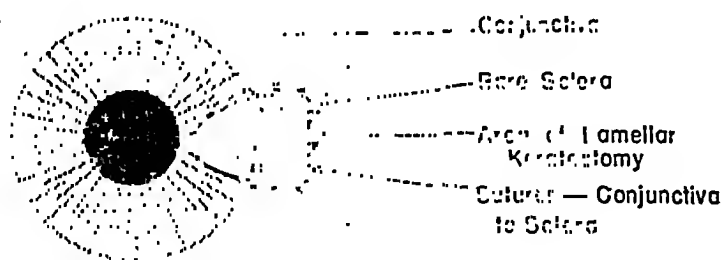


Fig. 5.—Appearance at completion of early operative procedure. Proliferation of vascularized connective tissue may invade the cornea at points *A* and *B*.

rise to neovascularization, which marred an otherwise perfect result. The Luns-gaard knife or a corneal splitter, therefore is preferable to a sharp-pointed knife.

One often finds a few superficial bleeding points. These are touched with a cautery tip, as it is found that such areas may give rise to new blood vessels which may extend onto the cornea, although they do not necessarily have enough supportive connective tissue to alter the gross clarity of the cornea. The anterior ciliary vessels are studiously avoided.

At this point, the portion of the cornea previously involved by the recurrent pterygium and a large area of the sclera have been laid bare. The cut edges of the conjunctiva and Tenon's capsule lie loose. In almost all other operations recorded in the literature, this defect has been covered by sliding or free grafts of conjunctiva, by skin grafts, by mucous membrane grafts, by amniotic membrane grafts or by Tenon's capsule and its subconjunctival component mobilized from the adjacent regions. The distinctive feature of the procedure presented here is

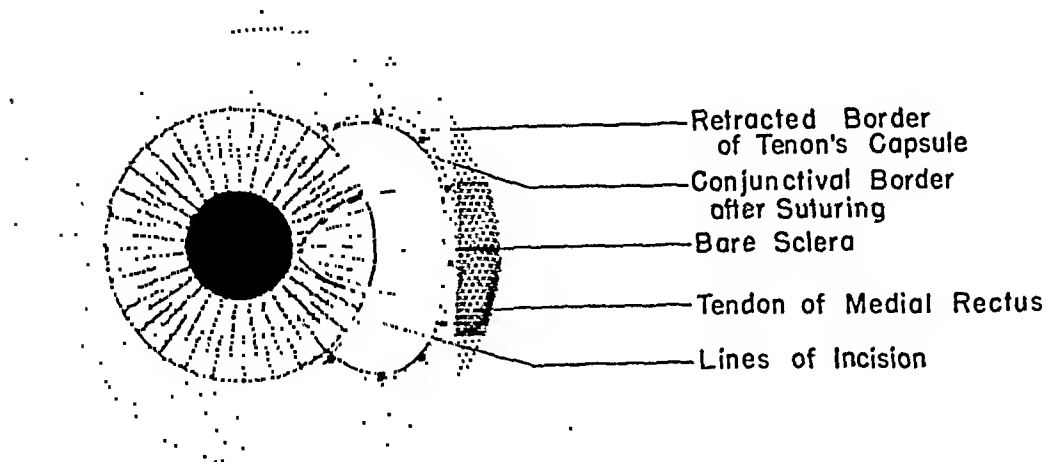


Fig. 6.—Appearance at completion of operative procedure, showing perilimbal incisions and recession of conjunctiva away from the area of keratectomy.

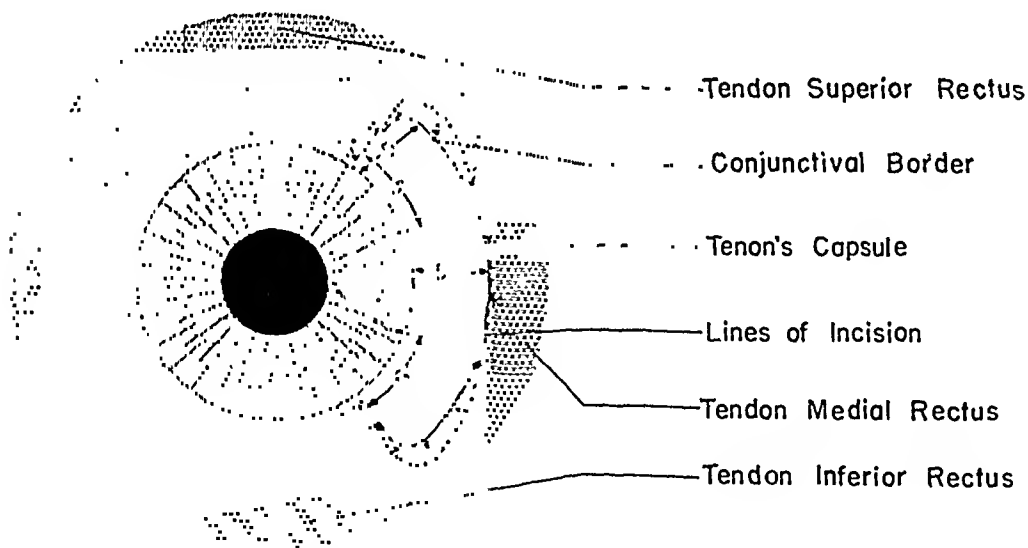


Fig. 7.—Diagram of second revision of procedure, showing radical recession of conjunctiva to prevent vascularization of cornea. The dimensions are expressed in millimeters.

that the conjunctiva is recessed and sutured to the sclera proper at least 5 mm. from the limbus and that the defect is allowed to epithelize by itself.

Because it seemed that blood vessels and connective tissue gave rise to the reformation of the scar tissue onto the cornea, an attempt was made to eradicate all such subepithelial tissue. Any graft heals by connective tissue binding it in place. Epithelium grows so rapidly and so close to the cornea and sclera that the wound heals before much connective tissue is formed. With kindly healing

and with the exercise of care to prevent irritation of the operative area, the stimulus to formation of subepithelial connective tissue is reduced to a minimum, and the process of repair is completed before granulation tissue is formed. One effects healing in this case not by "allowing the wound to granulate in" but by allowing the defect to become epithelized quickly.

With the aim of rapid epithelization in mind, certain details in suturing the conjunctiva to the sclera are watched with care. First, the outer layers of the conjunctiva are separated from the submucosa and Tenon's capsule as precisely as possible. The capsule is allowed to retract, while the thin, healthy conjunctiva alone is sutured as follows: A double-armed 0000000 black silk suture on atraumatic needles is used. One needle is passed through the outermost layers of the sclera with as little trauma as possible. The needles are then passed from within outward through the conjunctiva about 2 mm. apart, and the suture is then tied. This procedure flattens the conjunctiva against the sclera proper. Usually eight or ten such sutures are used. Care is taken to cover the insertion of the tendon of the medial rectus muscle, which has been disturbed as little as possible in the previous dissection. Tenon's capsule over the tendon is repaired if it has inadvertently been perforated or if it has been involved in the scar tissue mass. The importance of this precaution has been shown by Berens and Romaine.

In the early cases the conjunctiva was not incised along the limbus above and below the vertical limits of the recurrent pterygium. This angle was the site of the formation of new blood vessels. Later, a limbal incision was made 3 mm. above and below the head of the pterygium and the suturing completed, as shown in figure 6. This was usually satisfactory, but this angle also tended to be too acute in some cases. Hence, more mathematically logical incisions can be made 5 mm. above and below the limbal junction of the keratectomy site. This allows recession of the undermined conjunctiva 5 mm. from the limbus at all points and gives an angle of almost 90 degrees. The conjunctiva from point *A* is then sutured to the sclera, 5 mm. away (fig. 7). This, of course, makes a small ruffle of redundant conjunctiva above this area, but it is of no consequence, merely furnishing deeper fornices, a feature much to be desired in the cases in which symblepharon has produced ptosis and limitation of motion. It may be emphasized again that no limitation of motion results from this procedure, because, although conjunctiva (really epithelium) is tightly adherent to the globe nasally, the recession of conjunctiva and Tenon's capsule allows free mobility of the globe and eyelids.

When all the sutures are tied, the eye appears as shown in the sketches (fig. 8). Boric acid ointment, 5 per cent, is applied to the eyeball; the lids are carefully closed, and a pressure dressing is applied.

It is preferable to bandage both eyes for five to seven days, but this was done in only about half the cases. A tight pressure dressing is used.

*Postoperative Course.*—The dressing is left in place for four days, and the second dressing is reapplied in the same manner as the original one. Redressings are done every other day until the tenth day, when the sutures are removed. Staining with fluorescein is usually absent after the sixth or seventh day, sometimes being absent after the fifth day. In removing the sutures, care is taken not to incite bleeding or to disturb the tissues, lest more scar tissue be formed. If the subconjunctival tissue has been carefully dissected, there is little or no elevation peripheral to the sutures.

In the first cases, in which 100 r of unfiltered roentgen radiation was given on each of the first, second, third and fifth days (a total of 400 r), the dressing had to be removed for the treatments. The reaction

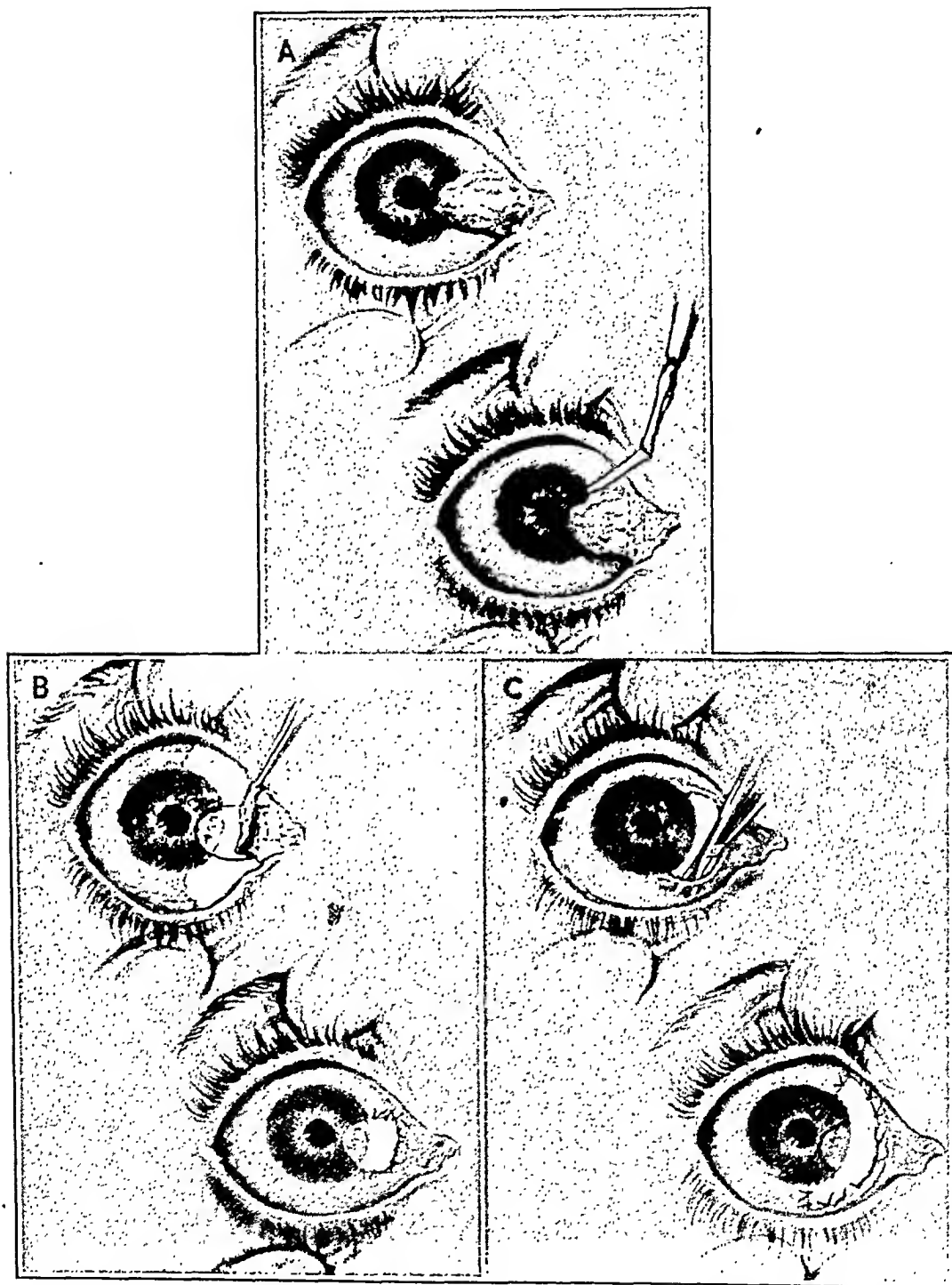


Fig. 8.—Crayon drawings showing the operative procedure for removal of recurrent pterygiums.

was greater as a result of this frequent manipulation. It is often unnecessary to consider any form of radiation therapy. It is now felt that the cornea should be observed carefully and that if any new blood

vessels appear treatment with beta radiation should be started promptly. This method is considered most satisfactory for handling vascularization in corneal transplants and it serves the same purpose for postoperative pterygiums.

Antibiotic therapy was not used, for we wished (1) to avoid allergic reactions, which might have an adverse effect and promote scar tissue formation, and (2) to determine whether this procedure is more likely to be complicated by infection than are other procedures. No clinical signs of infection occurred in any case. There has been no evidence of disturbance of nutrition of the cornea.

Atropine was used in about half the cases and no cycloplegic in the other half. In no instance did examination with the slit lamp show aqueous flare or cells, and synechias did not form. Hence, one may conclude that the use of a cycloplegic after operation is optional.

*End Result.*—For four to six weeks after operation the area nasal to the limbus appears too white, and close inspection reveals a slight concavity. Although the epithelium seems tightly adherent to the sclera over this entire area, blood vessels and a thin layer of supporting connective tissue grow toward the limbus, producing a more nearly normal-appearing bulbar conjunctiva.

The blood vessels tend to arborize as terminal branches, which end at or near the limbus. In a few cases the vessels reached the corneoscleral junction and then pursued a course parallel to it. In a few cases the vessels actually encroached on the cornea, but in only 1 case did a true recurrent pterygium develop. These vessels are readily obliterated by beta irradiation. In checking back on these cases, it was found that when any vessels passed the corneoscleral junction one of two factors present at operation had been responsible: (1) A little connective tissue had been left in place, (2) the conjunctiva had not been incised along the limbus far enough above and below the head of the pterygium to allow proper recession of the conjunctiva.

During the postoperative period these patients remained sheltered in an area (Pennsylvania) where the incidence of pterygium is low. This factor has undoubtedly been helpful. Whether such successful results would be obtained if this procedure were tried in South Africa, Panama, Egypt, the South Pacific or other areas where recurrence is known to be frequent remains an open question. However, other procedures tried at Valley Forge General Hospital were not effective, and the technic described here was eventually employed in every case of recurrent pterygium.

During the time of active military duty, it was impossible to make a satisfactory study of surgical methods other than those described in standard textbooks. The technic employed was serving its purpose well for the patients at one large hospital designated as a surgical eye

center. After the war it was found that not a few medical officers in the Army and Navy had found recurrent pterygium a problem in various parts of the world. More interest was then evinced in the method which had finally been successful in eradicating the multiple recurrences. Additional patients in both civilian and Army practice have been seen with similar lesions requiring treatment.

A thorough review of the literature was therefore undertaken. The results of this review have been condensed in order to bring up to date the pertinent data regarding pterygium under the headings of incidence, etiology, pathology, the causes of recurrence and the surgical treatment of both primary and recurrent pterygium. These topics are discussed briefly in relation to the surgical technic described in this paper.

While the technic was original so far as I actually knew, it is interesting, although not surprising, that the salient features were described independently by various authors about fifty years ago. What one now has is a combination of surgical principles and technical details described piecemeal long ago and apparently neglected over a considerable span of years.

#### HISTORY OF SURGICAL TREATMENT OF PTERYGIUM

The historical aspects of pterygium therapy are interesting in that there has been no gradual evolution to an optimum method, in keeping with the advances in general or ophthalmic surgery. Only those procedures which are similar to the one described in this paper are reviewed here. The remainder of the history of the surgical treatment has been omitted.

Boeckmann, in 1897, reported a procedure which he had used for fifteen years. He regarded excision as mutilating, the only excuse for it being that it was followed by good results! He compared the surgical treatment of pterygium with that of a fracture: The pterygium is a dislocation of conjunctiva, which requires reposition and fixation. He dissected the head from the cornea and from the sclera, excised all subconjunctival connective tissue and sutured the retracted border of the conjunctiva to the medial rectus muscle at its insertion. This left the conjunctiva in direct contact with the sclera and a triangular area of denuded sclera adjacent to the fresh corneal wound. He depended on tight adhesion between the conjunctiva and a rapidly forming cicatrix "to prevent recurrence for all time."

Lopez, of Habana, in 1898, advocated excision near the base, strangulation of the base, incisions bordering the limbus above and below the pterygium and dissection of these portions of the conjunctiva to prevent their adhesion to the denuded cornea. He used no sutures, simply leaving the borders of the conjunctiva to retract until after the corneal epithelium had regenerated.

Steiner, in 1911, described a new operation which he used in 7 cases of pseudopterygium, a lesion which, of course, is much like many recurrent pterygiums. He dissected the pseudopterygium from the cornea and sclera down to the fornix. He recessed the head and fastened it in the upper (or lower) fornix, using Snellen type sutures to fix it there and to deepen the shallow fornix. He left the sclera bare, to be covered with epithelium in eight or ten days. He stated that little by little, even after the corneal and scleral defect had healed, this transplanted margin of the conjunctiva slowly crept toward the cornea, and in some cases passed a little beyond its margin. However, in no case did it reach the center of the cornea to disturb vision, as before. There were no ill effects. He stressed the advantage of not sacrificing any conjunctiva, but of using it for deepening the conjunctival sac by recession of the border.

Mendoza, in 1931, described his treatment of recurrent pterygium with reduction in size of the conjunctival sac and restricted ocular mobility. He recessed the entire pterygium, sutured the head to the episclera and left the bulbar wound open. He made no mention of excising any scar tissue, although his procedure was successful in patients who had had several previous operations, including conjunctival transplants and grafts of labial mucous membrane.

In Busacca's procedure, described in 1938, it is difficult to follow the combination of transplantation, submucous resection, grooved incision near the caruncle and double cauterization of the area of sclera left bare between the margin of the pterygium and the limbus. However, he effected a recession of 3 to 4 mm. of the conjunctiva from the limbus and left an area of bared sclera to become epithelized. He reported recurrences.

These procedures are similar to the technic presented in this paper in two particulars: in recessing the conjunctiva to deepen the fornices or to prevent its adhesion to the denuded cornea, and in leaving a portion of the sclera bare, to become epithelized. These procedures differ in the over-all extent of the recession, in failure to excise all episcleral connective and scar tissue and in not suturing the conjunctival border to the outer layers of the sclera proper—all features considered of prime importance in preventing the late creeping up of vascularized connective tissue under the epithelial covering of the sclera. Dr. Arnold Knapp stated that he learned early the advisability of suturing the tissues to the sclera.

D'Ombrian has recently published an account of his extensive experience in the surgical treatment of 1,500 primary pterygiums in Australia. In general, he advocates leaving bare sclera to become epithelized after excising the head of the pterygium and all subconjunctival tissue as

far nasally as the plica semilunaris. D'Ombraïn uses no sutures, nor does he recess the conjunctiva above and below the vertical borders of the pterygium. His account is concerned mostly with operations on primary pterygia. He stated, "This technique may be successfully used in recurrent pterygium but in cases of second recurrence the free graft method . . . should be used." It would be interesting to see what results he might obtain in Australia by adding to his procedure the refinements described for cases of multiple recurrence. It was gratifying, indeed, to learn of D'Ombraïn's excellent results with his technic, an operation which is basically the same as that advocated in this paper.

Lombardo recently described recession of the conjunctiva for pannus of trachoma but made no mention of pterygium.

No entirely satisfactory single explanation for recurrence of pterygium has been brought forth. From the surgical standpoint, recurrence following operation has been attributed by various authors to the following factors: (1) incomplete dissection of the head of the pterygium from the cornea; (2) incomplete or impermanent removal of the original pterygium tissue from the area of the palpebral fissure regardless of the method employed; (3) remnants of connective tissue left adjacent to the corneoscleral junction at operation; (4) failure to have healthy conjunctiva extending to the limbus. Some authors have stated the belief that it is essential to have the conjunctiva approximate the corneoscleral junction precisely; others allow it to overlap; a few have stated that it is wise to leave a small gap between the border of the conjunctiva and the corneoscleral junction. Only a very few authors have recommended actual recession of the conjunctiva, and then usually in operation for recurrent lesions.

In addition to the first three points listed in the preceding paragraph, the following factors are held responsible for repeated recurrences: (1) failure to excise all scar tissue from cornea and episclera; (2) failure to occlude all blood vessels in the area of the recurrence; (3) reexposure after operation to the same factors which seemed to cause the original pterygium (that is, the patient remains in the same environment); (4) failure to suture the conjunctiva to the sclera; (5) failure to recess conjunctiva at least 5 mm. from the limbus; (6) too early reoperation; (7) use of grafts which are too thick, the extra thickness denoting vascularized connective tissue, which permits recurrence.

McReynolds, Ryerson, Francis, Pochissoff, Hirschberg and Mendoza described cases of particularly severe recurrent lesions. Gifford, of Omaha, cited Herman Knapp as saying that no operation should be performed for severe recurrent pterygia. Ryerson avoided sur-



gical intervention in some cases in which the pupillary area of the cornea was involved. He employed optical iridectomy, citing Noyes's statement that this might be the best method of dealing with an extremely severe lesion, although Noyes had added, "but I have never seen such a condition."

McReynolds, when asked by some of his colleagues what he did in severe cases with multiple recurrences, replied that he "regretted that the answer was not more favorable." After stating that he had tried thoroughly every imaginable method of destroying the recurrent growth, he eliminated all chemical and electrical methods as ineffective, since "they lead to severe reaction which in turn produces a correspondingly large amount of scar tissue, the evil genius of ophthalmic surgery." He advocated complete excision of all scar tissue, with preservation of the conjunctiva, which he sutured firmly to the sclera. Presumably he sutured it at the limbus, as he stated that his method was satisfactory when there was adequate conjunctiva, and used skin or mucous membrane when there had been too much destruction of conjunctiva. In none of his papers did he mention leaving the sclera bare to become epithelized. He concluded, "Finally there are some cases in which there has been so much destruction of tissue and so much scar formation that one might just as well refrain from any operative procedure."

These four opinions emphasize the obstinacy of recurrent pterygium in some cases. It is noteworthy that none of the authors cited attempted recession of the conjunctiva, as done by Boeckmann, Steiner, Busacca, Mendoza and me, and that none recorded more recurrences in any one patient than occurred in a case of the present series. It does not seem logical to avoid surgical treatment in the severest cases. It might be better in some cases to avoid surgical intervention for minor pterygium in the first place.

*Radiation Therapy.*—Radiation therapy has been employed by various men (1) in treatment of primary pterygium, (2) in treatment of recurrent pterygium and (3) as a postoperative measure to prevent recurrence or to eliminate vascularization of the cornea. It is generally agreed that the eye should not be subjected to any form of radiation unless there is good reason for so doing. Adequate protection of all parts of the eyeball not requiring actual treatment is essential. The dose should be the minimal effective one.

Reports of its use should include a statement of all the radiation factors: type of rays, number of roentgens, size of portal, target skin distance, time of application, type and thickness of filters, kilovoltage, milliamperage and half-value layer. Most reports do not give all this

information. In checking the roentgen and beta radiation given to some of the patients in this and in other series, I have been unable to determine all the radiation factors.

**Roentgen Radiation:** The results of using four applications of 100 r of unfiltered roentgen rays were disappointing, and such treatment was abandoned. Castroviejo reported much better results after using 1,500 r and stated that this dose prevents the formation of and eradicates new blood vessels in corneal transplants and after lamellar keratectomy.

**Beta Radiation:** The use of beta radiation has been very encouraging. It should be noted, however, that the bulb as used in some hospitals delivers as much as 10 per cent of gamma rays. Although the application time is short, it is felt that some danger exists and that treatment should be given only by persons skilled in the technic of irradiation.

The Phillips tube as employed at the Hospital of the University of Pennsylvania seems a well regulated, safe, precise method of delivering radiation. Some of the patients in this series were treated through the courtesy of Dr. F. H. Adler. No undue reaction occurred. The treatment was available when needed. New blood vessels were unquestionably destroyed when treated soon after their appearance. Other patients were treated under the direction of Dr. Charles Iliff, in Baltimore, according to the technic published by him.

While not enough data are available, it seems safe to state that beta radiation is not effective in completely eradicating primary or recurrent pterygium. It was used prior to surgical treatment in several cases of this series to hasten occlusion of vessels in heavily vascularized recurrent pterygium. The results were better after operation because the limited penetrating power of beta radiation makes its use more effective after the bulk of the tissue has been removed. Later observation leads one to feel that preoperative irradiation should be avoided. Grenz ray therapy was not employed.

Iliff reported successful treatment in 17 of 18 cases of primary pterygium, operation being required in only 1. He published no illustrations. Ruedemann showed colored photographs of patients treated with beta radiation. The end results appeared to be much less extensive corneal involvement and blanching of all blood vessels. He stated that for larger lesions he combines operation and beta irradiation. Truman has used a similar technic.

To summarize, it is generally felt that, of all methods of radiation therapy, beta irradiation offers the greatest benefit and that its effects are greatest when it is used as a postoperative measure to eradicate newly formed blood vessels in the cornea or those which seem about

to encroach on the cornea. Its use is advised when such blood vessels are found on examination with the slit lamp, and then prompt treatment is advocated. One is wise to make advance arrangements for beta irradiation during the period following operation for recurrent pterygium.

In order to test the practicability of the operative technic presented in this paper, and to be certain that the good results obtained were not simply due to good fortune, several other ophthalmologists have employed it. Their results paralleled those reported here.

#### SUMMARY

An operative technic developed to eradicate severe recurrent pterygium is described, and its results in a group of Army patients with from one to twelve recurrences are reported. Some of the patients had symblepharon, ptosis and limitation of mobility as a result of the extensive scar tissue.

The results were good after other procedures had failed to prevent recurrence. Although the series of patients is small the procedure is therefore offered for trial by other surgeons with the hope that it may be of value in regions where recurrences are more frequent and more troublesome. The technic is simple and safe, and the essential features are based on logical surgical principles.

This procedure consists, in brief, of lamellar keratectomy, submucous resection of all scar tissue and recession of the conjunctiva by suturing it to the sclera proper at least 5 mm. from the corneoscleral junction, the denuded cornea and sclera being allowed to become epithelized. Beta irradiation is used after operation when it is necessary to control vascularization. This simple technic has also been found suitable for excision of pseudopterygium and epibulbar tumors, repair of symblepharon and removal of superficially vascularized corneal scars.

Recession of the conjunctiva permits deepening of the contracted fornices, with consequent relief of ptosis, symblepharon and diplopia. Revascularization is likewise avoided. No ill effects have been observed from allowing the denuded cornea and sclera to become epithelized.

Although this procedure was developed without known precedent, it was not surprising, on a review of the literature, to find that it is a combination of surgical principles and technical details most of which had been described piecemeal many years ago and then neglected over a considerable span of years. The literature is reviewed, and the information on the incidence, etiology, pathology, causes of recurrence and surgical treatment of primary and recurrent pterygium is presented in condensed form.

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# EMBRYONAL CATARACT ASSOCIATED WITH INTERSTITIAL KERATITIS AND SYPHILITIC CHOROIDITIS

Report of a Case

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THE OCCURRENCE of an embryonal cataract associated with interstitial keratitis and syphilitic choroiditis is extremely rare, only 2 previous cases having been listed so far as I have been able to determine. Vogt,<sup>1</sup> who described 1 of these cases, suggested that all instances of such a condition be reported whenever observed, since the cause of this lenticular opacity has thus far not been satisfactorily determined. He stated that among the features not yet clearly understood are the reason for the coloration of the opacity, the relation of the opacity to interstitial keratitis, the eventual progression of this cataract to complete maturity and its mode of development. He did not list this opacity with the complicated cataracts, for he assumed that the disturbance in the lens occurred early in life and first manifested itself as a subcapsular opacity, which subsequently was pushed deeper into the lens through deposition of normal, healthy lens fibers between the capsule and the opacification.

Blaauw<sup>2</sup> reported a case as "circumscribed lamellar lens changes probably inherited." His patient, aged 35, presented an opacity in each lens which was yellow and cloudy, approximately 4.5 mm. in diameter and located within the adult nucleus. In cross section there was a cloudy, yellowish ring completely surrounding the embryonal nucleus. The ring appeared to become thicker at both its superior and its inferior extremity through a process of widening and flattening of the bands. The ring completely surrounded the nucleus, suggesting a globular body. The clear interval was normal, as were both the anterior and the posterior Y's.

The patient reported by Vogt,<sup>1</sup> a woman aged 37, had had two attacks of interstitial keratitis. Her father had had bilateral choroiditis. The biomicroscopic changes in the daughter's lens were interesting but not easy to explain. The abnormality occurred between the border of the middle and that of the posterior third of the lens. The change was

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1. Vogt: *Spaltlamp Microscopie*, Berlin, Julius Springer, 1931, vol. 2, p. 958.

2. Blaauw, E. E.: *Circumscribed Lamellar Lens Change Probably Inherited*, Arch. Ophth. 54:305 (May) 1925.

present in the axial region. The opacity was whitish yellow to red yellow and was concavely saucer shaped, occupying the position of one of the discontinuation zones. The opacity was bilateral. The posterior capsule of the lens was relatively flat, whereas the anterior capsule was highly arched. At the time of the acute flare-up of the interstitial keratitis, the lenticular disturbance was subcapsular, but as healthy lens fibers were laid down between the capsule and the opacity the cataract was pushed deeper into the lens substance.

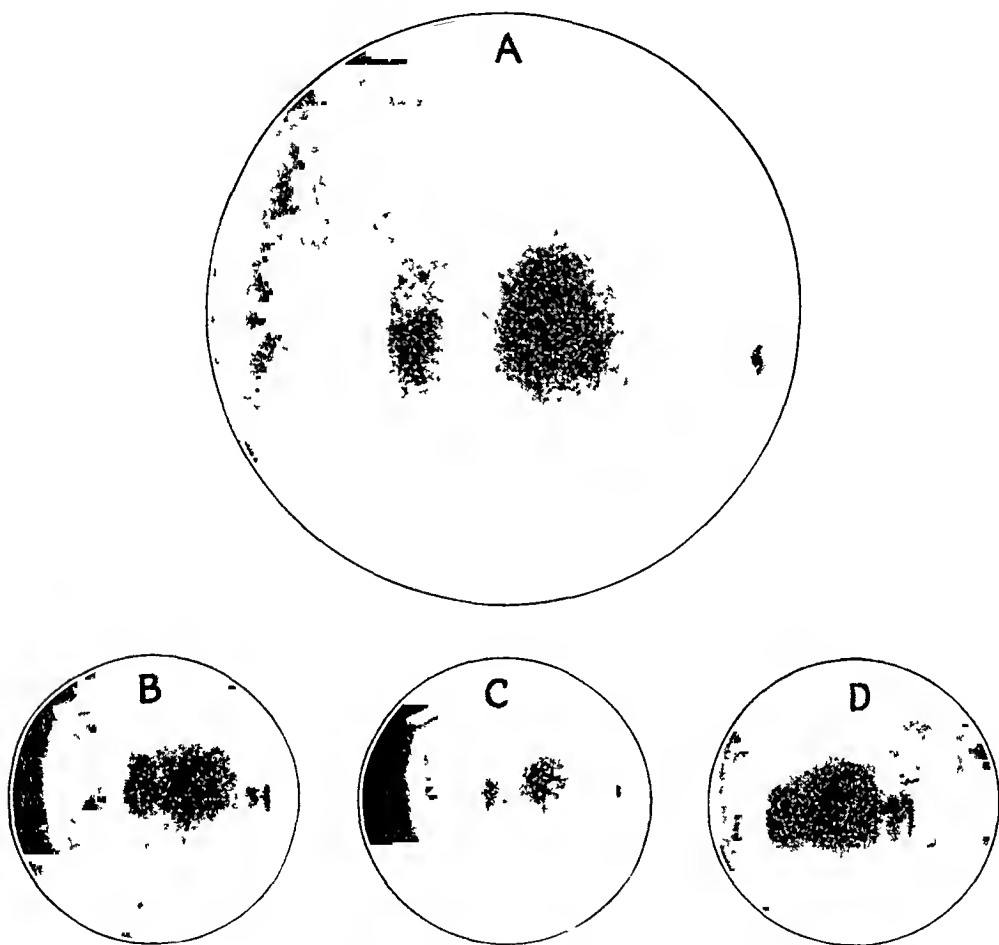


Fig. 1.—*A*, enlarged photograph of the slit beam in passing through the eye. *B*, *C* and *D*, photographs without enlargement, showing the wide beam, narrow beam and light exposure, respectively.

#### REPORT OF CASE

The patient was born at full term, although weighing only  $3\frac{1}{2}$  pounds (1,584 Gm.) at birth. The mother was married at 17 years of age to a man fourteen years older than herself. There was suspicion of a syphilitic infection on the paternal side. Separation followed shortly after the birth of the patient. The child was born a blue baby, but apparently after a few days no abnormality was noted. As long as she could remember, her vision had been much poorer than that

of other children. She remembered that after securing glasses at the age of 6 she still was unable to see the school blackboard and that a special desk was placed at the front of the room in order to aid her. Glasses were frequently changed until she was 16 years old, at which time she was told by her ophthalmologist that nothing further could be done for her vision. She then began to make the usual "rounds," encountering great disappointment in her quests for visual improvement. Eventually, she was hospitalized at Philadelphia, where the diagnosis of interstitial keratitis was offered. The etiologic factor remained unknown to the patient; however, she was referred to her family physician for biweekly intramuscular injections of arsphenamine. This treatment was continued for a long time, several separate series of injections being given. At the age of 21 a recurrence of her ocular trouble further incapacitated her. The corneas became grayish, with further visual

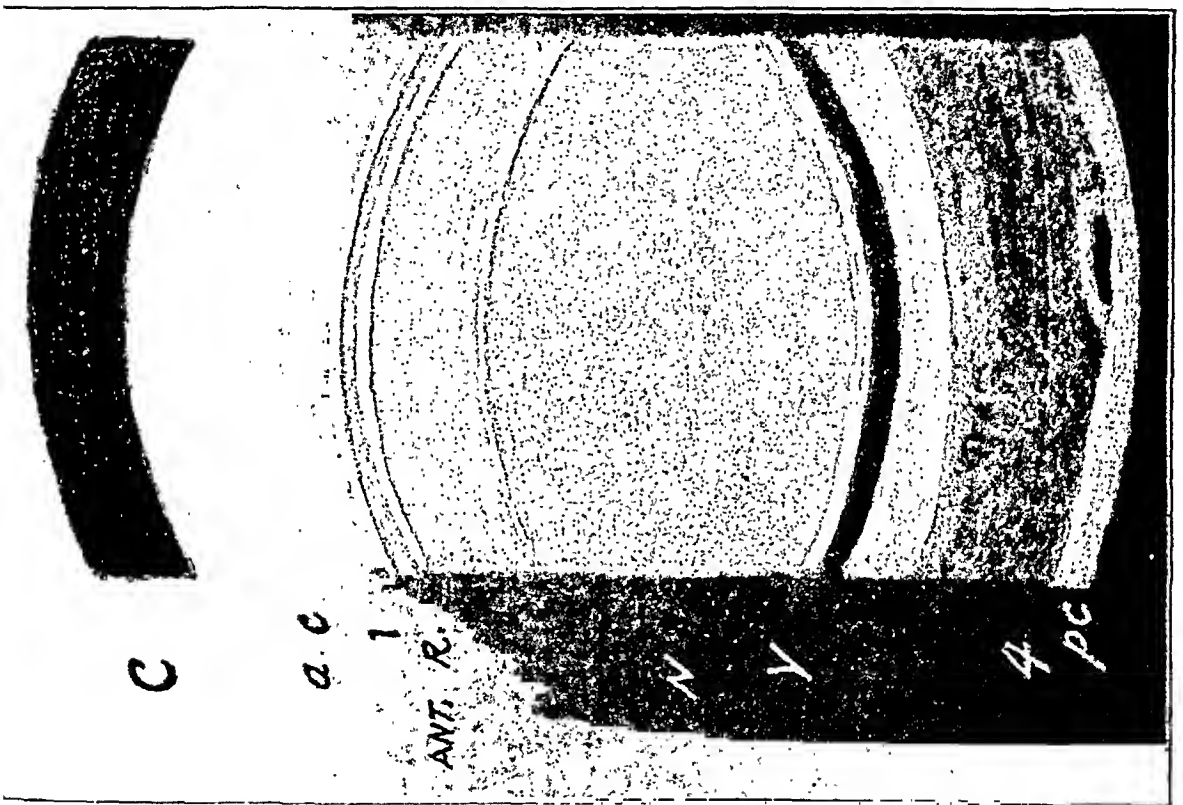


Fig. 2.—Diagram explaining figure 1: *c*, the cornea; *ac*, the anterior chamber; *1*, the anterior capsule; *ant. r.*, anterior reduplication band; *N*, nucleus; *y*, yellow ring; *4*, complicated cataract, and *pc*, posterior capsule.

reduction. After she had completed the course of injections, her eyes cleared considerably. She had observed that her ocular condition became worse during such critical periods as adolescence and the menopause (following hysterectomy).

Physical examination revealed that vision in the right eye was 2/200, correctable to 20/200 with  $-10.00$  sph.  $\ominus -7.00$  cyl., axis 165. Vision in the left eye was 3/200, correctable to 20/25 with  $-12.00$  sph.  $\ominus -7.50$  cyl., axis 165. There was a slight suggestion of exophthalmos, the Hertel exophthalmometer reading being 21 mm. for each eye.

There was no anomaly of motility, excursions of muscles appearing normal in all the cardinal directions of gaze. The pupils reacted promptly to light and in accommodation. The cornea of the right eye showed typical *Glasleiten* bodies. For the most part, these occupied the superior temporal quadrant of the right

cornea and were arranged in the form of a delicate network. They did not extend into the anterior chamber to any degree. They were transparent and rather definitely round in cross section (Duke-Elder<sup>3</sup>). No such change was noted on the cornea of the left eye or over the remaining area of the right cornea. The anterior chambers were of moderate depth. The iris was not remarkable in either eye.

The anterior capsule of each lens showed an increase in the number of lenticular spherules, particularly in the lower peripheral portion. The anterior reduplication band was not unusual. No disturbance or irregularity was demonstrable between this band and the anterior capsule. A rather wide clear zone extended up to the anterior surface of the embryonal nucleus. At this surface a dense, yellowish band was discernible; this band as seen in cross section fanned out in thickness toward the periphery but completed a circle of communication with the similar, but denser, band present in the same position in the posterior portion of the lens. The area between this yellowish ring was still fairly clear in the left eye, but in the right eye its appearance was identical with that of a nuclear cataract. In the right eye the anterior and posterior Y's appeared practically normal, whereas in the left eye these landmarks seemed like black Y's in a yellowish center. In the right eye a yellowish reduplication line was present just beyond this postembryonal band, which band was slightly thicker than the line just anterior to it. It had a diagonally streaked, hatched appearance. This reduplication line could not be made out in the posterior area of the lens in the left eye. Beyond these lines the lens appeared fairly clear until just anterior to the posterior capsule in the axial region, where appeared a series of polychromatic, crumblike, lustrous bodies, more pronounced and more extensive on the left side than on the right. This complicated cataractous change did not extend very far peripherad.

When viewed by direct illumination, these changes in the lens appeared like two extremely well-delineated, miniature nuclear cataracts, about 5 mm. in diameter, suspended in an area of clear cortex. The most striking feature about the opacities was the manner in which they were bordered or outlined. They looked just as though they had been suspended within a picture frame (figs. 1 and 2).

The extreme periphery of the fundus of each eye revealed an old healed choroiditis. This peripheral annular disseminated chorioretinitis was somewhat different in the two eyes. In the right eye the changes were primarily in the temporal periphery and consisted of small round black foci with eccentric whitish centers grouped together. There were also several larger, lobulated masses with no centers. In the left eye the annular pigmentation was much less extensive and occurred in groups, with no signs of lesions with white centers. The choroidal lesions appeared characteristic of congenital syphilitic annular chorioretinitis of the grouped pigmentation type. The *Glasleiten* bodies of the right cornea also suggested a congenital syphilitic origin.

#### COMMENT

From a study of this isolated case, it would seem that the presence of these changes in the lens should be anticipated in cases in which annular chorioretinitis and *Glasleiten* bodies of the cornea coexist, and that it

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3. Duke-Elder, W. S.: Text-Book of Ophthalmology, St. Louis, C. V. Mosby Company, 1938, vol. 2, p. 1876.

should be considered a finding of diagnostic import. The location of this type of band within specific zones of the lens is, of course, indicative of a nutritive disturbance of the lens at a period of syphilitic recrudescence. The implication may be that of an allergic response in tissue capable in each instance of reacting in a specific way, i. e., the avascular cornea responding in one manner, as only an avascular tissue can react, and the lens being organ specific and responding as would be anticipated of a highly avascular tissue. The annular intensification band in the lens is not unlike "annular rings" elsewhere in the plant and animal kingdoms. It connotes a period of temporary arrest in growth, and its cross sectional thickness is an indication of the duration of the altered state of the reacting organism. The predilection for the posterior portion of the lens is concerned with the capsulolenticular barrier and the relative intensities of the inflammatory reactions in the anterior and posterior ocular segments. In other words, if the inflammatory process is of equal intensity in the choroid and in the cornea, the annular ring should be more pronounced in the posterior portion of the lens, for passage of noxious products through the posterior portion of the lens should be less restricted. Thus, the posterior accentuated band should be anticipated. This band may also be of diagnostic import, since the conditions which may lead to its formation are necessarily limited. This lesion, like many other lesions, is not uncommon; its recognition will go hand-in-hand with an increase in the number of cases reported.

There are two other points which this case illustrates. The method of refraction in similar cases has no relation to glasses previously worn by the patient or to the retinoscopic findings. The patient herself discovered that her vision could be improved tremendously by placing her reading glasses over her distance glasses (left eye). This correction represented approximately the following prescription:

Near	Right	Left
Distance	No improvement:	
		— 4.50 sph. $\odot$ —3.50 cyl., ax 165
		— 7.50 sph. $\odot$ —3.50 cyl., ax 165
		= —12.00 sph. $\odot$ —7.00 cyl., ax 165;
		20/25 visual acuity

The second noteworthy point in this case is the aggravation of preexisting lenticular opacities at the time of one of the physiologic periods of stress (i. e., adolescence and the menopause). This point, of course, is well known but bears repetition, especially if presumptive evidence can be offered to establish such a claim.



Von Szily <sup>4</sup> has emphasized the promising opportunity of gaining a deeper insight into general pathology through observation of the changes in the lens, a structure which may be regarded as a complex group of cells forming an organ of such genetic uniformity as is found nowhere else in the body. This structure, living under such unusual conditions and composed of cells of such various ages, may show changes which bespeak alterations in body fluids at a specific time in life.

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4. von Szily, Ridley and Sorsby: *Modern Trends in Ophthalmology*, London, Butterworth & Company, Ltd., 1940.

## VISION OF ALBINOS

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ALBINOS have been known and described as such since very early times, but, unfortunately, the condition has been considered an anthropologic and genetic problem rather than a medical one. Albinism is a complex condition which probably includes more than just a lack of pigmentation.<sup>1</sup> It is usually divided into complete albinism and partial albinism, often called albinoidism or leukism (Gates<sup>2</sup>). Complete albinism, which will be referred to simply as albinism, is a genetic recessive character, transmitted by a partially sex-linked mosaic of genes (Castle and Allen<sup>3</sup>). Since the condition seems to be found more commonly in men, it was thought at one time to be semifatal to women, but there is no evidence for such an assumption. Albinism is characterized by pigmentless hair, skin and eyes and by ocular defects. Ametropia, astigmatism, nystagmus, photophobia and amblyopia are almost invariably all present. With age, albinos not uncommonly acquire more pigment (Pearson, Nettleship and Usher<sup>4</sup>).

Albinoidism is genetically dominant and regional in character. It may be as localized as a shock of white hair or as general a condition as to be almost undetectable from albinism. Generally, the hair and skin are slightly darker and the texture of the hair is less fine than they are in complete albinism. Affected persons have photophobia but no ocular defects. Because of this absence of ocular involvement, albinoidism will not be considered in this paper.

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1. Clark (Tr. Am. Ophth. Soc. 42:250-262, 1944) maintained that albinism is a much more widespread defect than just a lack of pigment and concomitant foveal impairment. He found that the condition may also be marked by the presence of lesions of the central nervous system. Neurologic examinations will be made on as many subjects in this series as practicable to see whether any such lesions can be detected.

2. Gates, R. R.: Human Genetics, New York, The Macmillan Company, 1946, vol. 1.

3. Castle, W. E., and Allen, G. M.: Proc. Am. Acad. Arts & Sc., vol. 38, no. 21 (April) 1903.

4. Pearson, K.; Nettleship, E., and Usher, C. H.: Monograph on Albinism in Man, London, Dulau & Company, 1911-1913, pts. 1 and 2.

Albinism seems to be a relative lack, rather than complete absence, of pigment, the variations in pigmentation being greatest in the eyes. The question how much pigment an albino may have in his eyes and where it occurs has been a highly controversial one. Duane<sup>5</sup> stated that the pigment of the pigment epithelium is merely scanty in albinos. Elschmig,<sup>6</sup> in his albinos, observed pigment in the pigment epithelium of the sphincter of the iris, the ciliary body and the retina but no pigment in the iris stroma or in the choroid. Gilbert<sup>7</sup> noted pigment throughout the pigment epithelium. Schanz<sup>8</sup> stated that in all albino eyes which had been examined, without exception, pigment had been found in the pigment epithelium, even when the other ocular parts and the rest of the body were entirely free from pigment. Neame and Williamson-Noble,<sup>9</sup> however, asserted that in the albino there is no pigment in the pigment epithelium. Collins and Mayou<sup>10</sup> stated that in the albino infant's eye there is no trace of pigment, but that in every adult albino eye thus far examined traces of pigment have been observed. Pigment has been found in the retinal epithelium when it is entirely absent from the stroma of the iris, ciliary body and choroid. Pigment may be entirely absent from the stroma of the uveal tract except in the choroid of the macular region. Gates<sup>2</sup> stated that in total, or complete, albinism the pigmentation of the eye varies, traces of pigment being present nearly always in some parts of the eye.

It is apparent from this review that any subject examined as an albino in a series of visual tests, such as will be described, cannot be classified as an albino until after all the tests are completed. Unless the subject has both the relative lack of pigment and the distinctive visual defects he is not albino. Relative lack of pigment alone could mean that he was albinodic, or even merely blond; the visual defects alone might be caused by other conditions.

#### PRESENT INVESTIGATION

In the experiments which were carried out in this study a series of 16 subjects, considered albinos, was used. The purpose of the experiments was to describe and measure the vision of these persons by as many

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5. Fuchs, E.: *Text-Book of Ophthalmology*, authorized translation from the twelfth German edition by Alexander Duane, ed. 5, Philadelphia, J. B. Lippincott Company, 1917.

6. Elschmig, A.: *Arch. f. Ophth.* **84**:401-419, 1913.

7. Gilbert, W.: *Arch. f. Augenh.* **88**:143, 1920.

8. Schanz, F.: *Am. J. Psych. Optics* **4**:284, 1924.

9. Neame, H., and Williamson-Noble, F. A.: *A Handbook of Ophthalmology*, ed. 5, London, J. & A. Churchill, Ltd., 1944.

10. Collins, E. T., and Mayou, M. S.: *Pathology and Bacteriology of the Eye*, Philadelphia, P. Blakiston's Son & Company, 1925.

technics as was practicable and, if possible, to enhance their visual acuity and increase their ocular comfort.

The group was obtained with the cooperation of the New York Association for the Blind, the New York Board of Education and the New York Department of Health. The ages ranged from 7 to 45 (table 1). The testing was done at the Institute of Ophthalmology, Columbia-Presbyterian Medical Center, under the supervision of Dr. LeGrand H.

TABLE 1.—*Data on Age, Fundus, Vision and Glasses for 16 Albino Subjects*

Subject	Age, Yr.	Pigment Deficiency	Vision*		Glasses
			Right Eye	Left Eye	
1	45	Extreme	20/200 sc	20/200 sc	None
2	32	Extreme	10/200 sc	8/200 sc	None
3	30	Extreme	20/200 sc	20/200 sc	RE: +4.50 ( ) +0.50, ax. 90 LE: +4.50 ( ) +0.50, ax. 90
4	22	Moderate	10/200 cc	10/200 cc	RE: -14.00 ( ) -2.00, ax. 28 LE: -14.00 ( ) -2.00, ax. 68
5	13	Extreme	15/200 cc	20/200 cc	RE: +6.00 ( ) +2.00, ax. 90 LE: +6.00 ( ) +2.00, ax. 90
6	12	Extreme	20/70 cc	20/100 cc	RE: -11.00 ( ) -3.50, ax. 180 LE: -11.00 ( ) -3.50, ax. 180
7	12	Moderate	20/70 cc	20/100 cc	RE: +1.00 ( ) +2.00, ax. 35 LE: +1.00 ( ) +1.50, ax. 92
8	11	Extreme	10/200 cc	10/200 cc	RE: +0.25 ( ) -4.50, ax. 178 LE: -0.25 ( ) -3.25, ax. 178
9	11	Extreme	10/200 cc	10/200 cc	RE: +3.50 ( ) +2.00, ax. 180 LE: +3.50 ( ) +2.00, ax. 180
10	11	Mild	20/200 cc	20/200 cc	RE: +1.25 ( ) +3.00, ax. 77 LE: +2.00 ( ) +3.00, ax. 90
11	10	Extreme	20/200 cc	20/200 cc	RE: +1.50 ( ) +3.00, ax. 90 LE: +1.50 ( ) +3.00, ax. 90
12	9	Extreme	20/200 cc	20/200 cc	RE: +7.00 ( ) +1.00, ax. 95 LE: +5.00 ( ) +1.75, ax. 90
13	9	Extreme	10/200 cc	10/200 cc	RE: -1.50 sph. LE: -1.50 sph.
14	8	Extreme	20/200 cc	20/200 cc	RE: +0.75 sph. LE: +0.50 sph.
15	7	Extreme	15/200 cc	15/200 cc	RE: -2.50 ( ) +4.75, ax. 105 LE: -2.50 ( ) +5.25, ax. 77
16	7	Extreme	17/200 cc	17/200 cc	RE: -2.00 sph. LE: -1.75 sph.

\* The visual acuities indicated with "sc" are without correction; those with "cc," with correction.

Hardy. Each of the 16 subjects had an examination of the fundus by one of the ophthalmologists of the Institute. Thirteen were classified as having the typical extreme lack of pigment; 2 had somewhat more pigment; and 1, a boy, had sufficient pigment in the fundus to be called blond. Since the last 3 subjects had the same kind of ocular defects as the others, however, they too were considered to be albinos in the final analysis.

The visual acuity of the 16 subjects, with correction as prescribed, ranged from 20/70 to 8/200. Measurements were made for each eye,

using Snellen charts at standard distances and with standard illumination. The average acuity was approximately 20/200 (table 1).

Fourteen of the group wore glasses for distant vision and/or reading (table 1). A number of them, mainly children, considered their glasses more a burden than an aid. Many had sunglasses for outside wear, and several had their regular glasses slightly tinted. Nine of the subjects were hypermetropic and 5 myopic. Only 3 did not have astigmatic correction. According to Pearson, Nettleship and Usher,<sup>4</sup> refractive errors are found more frequently in albinos than in persons with normally pigmented eyes.

Each subject was tested for color blindness using the American Optical Company's Pseudo-Isochromatic Plates, revised edition; the Farnsworth Dichotomous Test, and the Bausch & Lomb model of the Rand anomaloscope. Standard conditions and technics were used in

TABLE 2.—*Color Discrimination\* of Albino Subjects*

Subject	Color Discrimination	Subject	Color Discrimination
1	Low	9	Low
2	Low	10	Deuteranomalous
3	Mild protanomalous	11	Normal
4	Normal	12	Normal
5	Low	13	Low
6	Normal	14	Normal
7	Low	15	Low
8	Low	16	Low

\* Color discrimination as based on examinations with the American Optical Company Pseudo-Isochromatic Plates, revised edition; the Farnsworth Dichotomous Test, and the Bausch & Lomb model of the Rand anomaloscope.

each case. Contrary to popular belief (Crafts and others<sup>11</sup>), albinos cannot be classified as color blind. As shown in table 2, 5 of the subjects had normal color vision, and 9 had low discrimination owing to poor acuity (no specific color blindness errors), while 1 subject was mildly protanomalous and 1 deuteranomalous. From this it is possible to say that albinos are likely to have low color discrimination due to poor acuity but are not more likely than the normal population to be specifically color blind.

Peripheral fields were measured with the Ferree-Rand perimeter, using illumination of 7 foot candles, a preexposure card and standard gray backgrounds. Each eye was measured for each 45 degree interval with 1 degree white, red and blue stimuli. The results are summarized

11. Crafts, L.; Schneirla, T.; Robinson, E., and Gilbert, R.: Recent Experiments in Psychology, New York, McGraw-Hill Book Company, 1938.

in table 3. In each of the 15 cases in which the fields were measured, white, or form, fields were contracted temporally beyond the minimum normal limits (Ferree, Rand and Monroe<sup>12</sup>), and in 7 cases the fields

TABLE 3.—*Peripheral and Central Fields\**

Subject	Peripheral Fields			Central Fields
	Form 1°	Red 1°	Blue 1°	
1	RE: Contracted temporally LE: Contracted	RE and LE: Contracted temporally	RE and LE: Contracted temporally	Relative scotoma 3/1,000 stimulus RE: 1.5°; LE: 1.0°
2	RE: Contracted LE: Contracted	RE and LE: Contracted temporally	RE: Contracted LE: Contracted	Relative scotoma 1/1,000 stimulus RE: 4.5°; LE: 4.0°
3	RE and LE: Contracted temporally	RE: Normal LE: Normal	RE: Normal LE: Normal	Absolute scotoma 1/1,000 stimulus RE: 1.0°; LE: 1.0°
4	RE and LE: Contracted temporally	RE: Normal LE: Contracted temporally	RE: Normal LE: Contracted temporally	Absolute scotoma 3/1,000 stimulus RE: 1.5°; LE: 1.5°
5	RE: Contracted LE: Contracted	RE: Normal LE: Contracted temporally	RE and LE: Contracted temporally	Absolute scotoma 1/1,000 stimulus RE: 2.0°; LE: 2.5°
6	RE and LE: Contracted temporally	RE: Normal LE: Normal	RE: Normal LE: Normal	Relative scotoma 1/1,000 stimulus RE: 4.0°; LE: 6.0°
7	RE and LE: Contracted temporally	RE: Normal LE: Normal	RE: Normal LE: Normal	Relative scotoma 1/1,000 stimulus RE: 2.5°; LE: 3.0°
8	RE: Contracted LE: Contracted	RE: Contracted temporally LE: Normal	RE and LE: Contracted temporally	Relative scotoma 1/1,000 stimulus RE: 6.5°; LE: 4.0°
9	RE: Contracted LE: Contracted	RE: Normal LE: Contracted temporally	RE and LE: Contracted temporally	Relative scotoma 1/1,000 stimulus RE: 3.5°; LE: 4.5°
10	RE and LE: Contracted temporally	RE: Normal LE: Normal	RE: Normal LE: Normal	Absolute scotoma 1/1,000 stimulus RE: 1.5°; LE: 1.5°
11	RE: Contracted LE: Contracted	RE: Contracted LE: Contracted	RE: Contracted LE: Contracted	Relative scotoma 1/1,000 stimulus RE: 2.0°; LE: 2.0°
12	RE: Contracted temporally LE: Contracted	.....	.....	Relative scotoma 1/1,000 stimulus RE: 1.5°; LE: 1.5°
13	RE: Contracted LE: Contracted	RE and LE: Contracted temporally	RE and LE: Contracted temporally	Relative scotoma 1/1,000 stimulus RE: 3.0°; LE: 4.0°
14	RE: Contracted LE: Contracted temporally	RE: Contracted temporally LE: Normal	RE: Normal LE: Normal	Relative scotoma 1/1,000 stimulus RE: 5.5°; LE: 6.5°
15	RE: Contracted LE: Contracted	.....	.....	Relative scotoma 1/1,000 stimulus RE: 4.0°; LE: 4.0°
16	.....	.....	.....	Relative scotoma 1/1,000 stimulus RE: 3.0°; LE: 2.0°

\* Peripheral and central fields as measured with the Ferree-Rand perimeter and the black meter tangent screen.

(both eyes) were contracted in all directions. Using the 1 degree red stimulus, the fields for 13 subjects were measured. Nine had contraction of at least one of their fields, either temporally or in all directions, while

12. Ferree, C. E.; Rand, G., and Monroe, M. M.: Diagnostic Scales for One Degree and 0.17 Degree Form Field Stimuli for Eight Principal Meridional Quadrants Taken Separately, Arch. Ophth. 6:518-535 (Oct.) 1931.

4 had fields (both eyes) as large as or larger than the minimum normal (Ferree, Rand and Monroe<sup>13</sup>). With the 1 degree blue stimulus, 8 of the same group had at least one of their fields contracted, either temporally or in all directions, while 5 had fields (both eyes) as large as or larger than the minimum normal. The only prediction from these data is that the form fields of albinos will be contracted, at least temporally.

It was most important during this perimetric work to watch the eyes of the subject continually because of the ever present nystagmus. It was not possible to eliminate the slight oscillation, but with frequent rest periods or, in the case of some of the younger children, by snapping the fingers in front of the fixation point, it was possible with repeated trials to obtain values which did not represent gross ocular movement. Since the oscillation could tend only to increase the fields as measured, it is thought that the values given err only in the direction of being too large.

Using a black meter tangent screen with a 1 mm. white stimulus (3 mm. in 2 cases), under illumination of 10 foot candles, the central fields were measured. As is shown in table 3, in every case there was a central scotoma, being relative in 12 cases (the test object became "smaller" or "dimmer") and absolute in 4 cases (the test object, in the last 2 cases a 3 mm. test object, disappeared). Subjects were not given any clue as to what would happen to the test object but were asked merely to tell what became of it. The sizes of the scotoma ranged from 1 to 6.5 degrees and were readily reproducible.

The amblyopia, or dimness of vision of albinism is probably due almost entirely to this central scotoma. Just why the central region should be more affected by the albinism than the other regions is not known. Neame and Williamson-Noble<sup>9</sup> called the condition impaired differentiation of the fovea. If it were that alone, it would seem that the fovea would have the same sensitivity as the surrounding area, rather than less sensitivity. A possible explanation might be that the albino infant is born with a normal fovea, but that the fovea atrophies because of overstimulation, the pigment being insufficient to control the entering light. According to Nettleship,<sup>14</sup> blindness due to overexposure to bright light is always localized to the macular region. If this is the case, it might be advisable to keep albino infants away from bright light until their eyes can be protected by one of the methods to be described later.

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13. Ferree, C. E.: Rand, G., and Monroe, M. M.: *Am. J. Ophth.* **16** (July) 1933.

14. Nettleship, E.: *Diseases of the Eye*, New York, Lea Brothers, 1900.

It was suggested by Wölfflin<sup>15</sup> in 1905 that the speed of dark adaptation may depend partially on the amount of pigment in the retina. Schirmer,<sup>16</sup> however, in 1890 had reported finding normal adaptation in 4 albinos, the Forster photometer being used for measurement. Stargardt<sup>17</sup> (1910), Mosso<sup>18</sup> (1914) and Takagi<sup>19</sup> (1926) also reported normal adaptation for albinos, although they did not use light adaptation before the measurements or use normal controls. Shaad<sup>20</sup> (1933) measured a group of 10 albinos and 13 persons with normal pigmentation, using the Nagel adaptometer, with preexposure to an illuminated screen (18.95 millilamberts) for five minutes. She took readings for each eye at one, five, ten, twenty and thirty minutes. Averaging the curves for the albino subjects and those for the normal subjects, she concluded that albinos adapt more slowly at first but become somewhat more sensitive by the end of the thirty minutes than do the normal subjects. Since she used a small group and took only five readings per eye, it is felt that her average curve for albino subjects cannot be considered as significantly different from the curve for normal subjects. Bunge and Heyn<sup>21</sup> (1938) measured the dark adaptation of 8 subjects with general albinism and 1 albinotic subject (in the latter the eyes were pigmentless, but not the body). The authors permitted light adaptation for fifteen minutes; they then took readings with the Engelking-Hartung adaptometer every minute for the first few minutes, and then every five to ten minutes up to forty-five minutes. They found both photopic and scotopic curves normal for all the subjects.

In the current study, dark adaptation was measured with the Hecht-Shlaer adaptometer under standard conditions for each eye of 13 subjects and for one eye of 2 subjects. In the case of a 7 year old subject it was impossible to measure dark adaptation. Readings were taken at approximately one minute intervals for thirty minutes. For 5 subjects the dark adaptation was normal (Mandelbaum<sup>22</sup>); for 5 the curves were somewhat irregular, with the final thresholds normal. For the other 5 subjects the final thresholds were from 0.1 to 0.5 log micromicrolamberts high

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15. Wölfflin, E.: *Arch. f. Ophth.* **61**:524, 1905.

16. Schirmer, O.: *Arch. f. Ophth.* **36**:121, 1890.

17. Stargardt, K.: *Arch. f. Ophth.* **73**:77, 1910.

18. Mosso, G.: *Ann. di ottal.* **43**:79, 1914.

19. Tagaki, R.: *Ztschr. f. Augenh.* **58**:436, 1926.

20. Shaad, D. J.: Dark Adaptation in Albinotic Eye, *Arch. Ophth.* **9**:179-190 (Feb.) 1933.

21. Bunge, E., and Heyn, W.: *Klin. Monatsbl. f. Augenh.* **100**:178-186 (Feb.) 1938.





22. Mandelbaum, J.: Dark Adaptation: Some Physiologic Considerations, *Arch. Ophth.* **26**:203 (Aug.) 1941.



(table 4). From these results, which agree for the most part with the previous work, it can be said that albinos have fairly normal adaptation, with both rods and cones functioning properly.

Nystagmus seems to be ever present in albinos. According to Pearson, Nettleship and Usher,<sup>4</sup> the nystagmus associated with albinism is no different from that caused by other deficiencies, abnormalities or diseases of the eye. Poor central vision, caused in this case by the amblyopia and/or central scotoma, allows the subcortical rhythm center, which is normally held in check by the cortex, to produce the involuntary rhythmic oscillations (Lorente de Nó and Berens<sup>23</sup>).

TABLE 4.—*Dark Adaptation\* in 16 Albino Subjects*

Subject	Normal Adaptation	Normal Atypical	Typical Shape Final Threshold High	Atypical Shape Final Threshold High
				
1	Right and left eyes	.....	.....	.....
2	Right and left eyes	.....	.....	.....
3	.....	.....	Right and left eyes	.....
4	.....	Right and left eyes	.....	.....
5	.....	Right and left eyes	.....	.....
6	.....	.....	.....	Right and left eyes
7	.....	Right and left eyes	.....	.....
8	.....	Left eye	.....	.....
9	.....	.....	.....	Right and left eyes
10	Right and left eyes	.....	.....	.....
11	Right and left eyes	.....	.....	.....
12	.....	.....	.....	Right and left eyes
13	Right and left eyes	.....	.....	.....
14	.....	Right and left eyes	.....	.....
15	.....	.....	.....	.....
16	.....	.....	.....	Left eye

\* Dark adaptation, as measured by the Hecht-Schlaer Dark Adaptometer, using standard conditions and techniques.

Usher (Pearson, Nettleship and Usher<sup>4</sup>) observed the frequency of nystagmus movements in 33 albinos. For 7 it was within the range of from 66 to 96 movements per minute; for 17, from 100 to 120 per minute, and for 9, from 121 to 156 per minute.

The nystagmus of a group of albino subjects was reported on by Ohm.<sup>24</sup> Over a period of years, he had measured the nystagmus of 31 subjects with pigmentless or defectively pigmented retinas. His

23. Lorente de Nó, R., and Berens, C.: Nystagmus, in Piersol, G. M.; Bortz, E. L., and others: *The Cyclopedia of Medicine, Surgery, and Specialties*, Philadelphia, F. H. Davis Company, 1939.

24. Ohm, J.: *Arch. f. Augenh.* 103:216-235 (June) 1930.

method, which he used in all his work on nystagmus (Ohm<sup>25</sup>), consisted in recording on a kymograph the movements of the eye by means of a fixed system, attached by a hook and string to the edge of the cornea. In all subjects he found uniformity in the direction of the movement, being horizontal in 27 and rotary in 4. There was, however, great lability in frequency and amplitude. Frequencies for the group ranged from 0.6 to 9.7 movements per second, and amplitudes, from 0.1 to 6.0 mm. Certain special conditions modified the movement. In general, looking to the left caused quick movements, or "rucks," to the left, with slower return movements; looking to the right caused the reverse. Looking straight ahead gave "dome"-shaped and "inverted dome"-shaped movements. In the light the nystagmus was more pronounced than in the dark.

This method has several sources of error. A weighted lever system is apt to give a distorted record, with lagging and overshooting. The trauma of attaching a hook to the edge of the cornea is likely to affect the results. Reliance solely on a Zeiss chin rest to immobilize the movements of the head is far from satisfactory.<sup>26</sup>

The nystagmus of the albinos in this study was described on the basis of observations and motion pictures taken at 10 frames per second with the use of infra-red illumination. Since the nystagmus was observed to have little, if any, vertical component in any of the subjects, only the horizontal component was measured, although the photographic records could be used to measure the vertical component as well.

The motion pictures of the nystagmus were made utilizing equipment designed for work in pupillography (Löwenstein and Friedman<sup>27</sup>). During the photographing (in a darkened room, with only infra-red light), the subject was told to look in the direction of a faintly lighted ground glass prism, 1 by 1.2 cm., at a distance of 30 cm., without attempting to focus or strain. The head was held by head and chin rests. Further to insure immobilization of the head, a tiny point of light was directed on a spot of ink dabbed on the nose. So long as the point of

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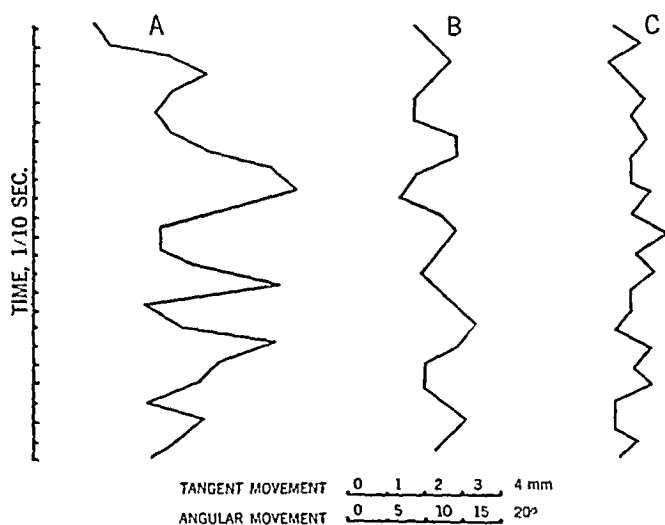
25. Ohm, J.: *Klin. Wchnschr.* 4:1286, 1925.

26. Adler and Fliegelman (Influence of Fixation on Visual Acuity, *Arch. Ophth.* 12:475 [Oct.] 1934) measured ocular movements using a tiny mirror attached to the temporal limbus. The beam of light reflected by the mirror was recorded photographically. This method is simple and seems superior to Ohm's but still has the factor of a foreign body on the eye.

27. Löwenstein, O., and Friedman, E. D.: *Pupillographic Studies: Present State of Pupillography; Its Method and Diagnostic Significance*, *Arch. Ophth.* 27:969 (May) 1942.

light remained fixed on the spot, it was assumed that the head was not being moved.

The nystagmus was measured (horizontal component) by projecting the developed film on a calibrated screen and plotting the position of the center of the pupil against time. In this way, movement of the pupil as projected on a line tangent to the vertex of the cornea was recorded. The optical system was such that the projected eyes were ten times normal size. Movement measured in centimeters on the screen could then be plotted as millimeters on the graph. Because of the impracticability of determining the straight-ahead position of the eyes, an arbitrary position was chosen in each case, and the relative movements were then plotted. Using Helmholtz' value for the average radius of the globe,



Short sections of graphs showing horizontal nystagmus movements as measured photographically with infra-red light. See text.

A (subject 15) is the graph for marked nystagmus; B (subject 12), for moderate nystagmus, and C (subject 5), for slight nystagmus. Comparative scales for tangent and angular movements appear below the graphs.

11.025 mm. (Helmholtz<sup>28</sup>), this tangent movement can be converted into angles of ocular rotation, 1 mm. very nearly equaling 5 degrees in the ranges used. Portions of typical graphs with scales for tangent movement and angular movement are given in the figure.

From the graphs made for the group, the maximum and average movements and the frequency for each subject were determined. (Voluntary movements, whenever present, could be distinguished by their

28. Helmholtz, H. L. F.: *Treatise on Physiological Optics*, ed. 3, translated from the German by J. P. C. Southall, Menasha, Wis., G. Banta Publishing Company, 1924, vol. 3.

amplitude and nonrhythmic occurrence.) The frequencies of the group ranged from 35 to 220 per minute. The maximum movements were as great as 9.5 mm. and as slight as 0.5 mm. The average movements ranged from 5 to 0.5 mm. (table 5). These values agree fairly well with Ohm's findings. From the size of the average movement it is possible to classify the nystagmus as marked, moderate or slight. It might be said that if the average movement is 1 mm. or less the nystagmus is slight; if less than 3 mm. but more than 1 mm., it is moderate; if 3 mm. or more, it is marked. In this group, then, there were 3 subjects with marked nystagmus, 3 with moderate nystagmus and 9 with slight

TABLE 5.—*Nystagmus in 16 Albino Subjects\**

Subject	Direction	Frequency, Min.	Maximum, Min.	Average, Min.	Amount	Aware- ness	Effect of Concentration on Movement
1	Horizontal	75	3	1.5	Moderate	No	Increased
2	Horizontal	220	2	1	Slight	No	Increased
3	Horizontal	180	3	1.5	Moderate	No	Increased
4	Horizontal	220	2	1	Slight	Yes	Increased
5	Horizontal	170	1.5	1	Slight	No	Increased
6	Horizontal	35	0.5	0.5	Slight	No	Increased
7	Horizontal	110	1	0.5	Slight	Yes	Increased
8	Horizontal	105	1.5	1	Slight	Yes	Increased
9	Horizontal	60	9.5	5	Marked	No	Increased
10	Horizontal	100	6.5	3	Marked	Yes	Increased
11	Horizontal	140	3	1	Slight	No	Increased
12	Horizontal	130	2.5	1.5	Moderate	Yes	Increased
13	Horizontal	110	2	1	Slight	No	Increased
14	Horizontal	120	1.5	1	Slight	No	Increased
15	Horizontal	120	5	3.5	Marked	Yes	Increased
16	Horizontal	...	..	..	.....	No	Increased

\* The nystagmus in the dark as measured photographically using infra-red light, with the subjects looking straight ahead but not fixating.

nystagmus. These values are for a darkened room only, with the subject looking straight ahead without straining or focusing. As is shown in table 5, concentration on an object at close (reading) distance increased the nystagmus for every member of this group.

By observation and questioning, it was possible to determine whether or not the subjects were aware of their nystagmus. Ten were not aware of the movement, while 6 were. Of the 6, 1, a girl, was able to modify, i. e., partially control, her nystagmus for very short intervals. I had previously noted this modifiability in another albino, and it seemed not to be correlated with either amount or frequency of movement.

Since albinos have little or no pigment in the sclera or the epithelium of the iris (or in the fundus), light enters through any part of the front of the eye, rather than through the pupil only, as in normally pigmented eyes. This diffuse light blurs the image formed by the light passing through the pupil and causes great discomfort in high illumination. It is typical of albinos to squint and shade their eyes in the

sunshine or in a brightly lighted room. Sunglasses serve only to reduce the total illumination falling on the eye, and when dark enough to reduce the squinting effectively, they reduce the already extremely low acuity. Pinhole goggles are not successful, since the subjects, with their ever present nystagmus, are unable to look through the aperture.

Several technics have been devised in the past in an effort to improve the vision of albinos by the removal of glare while not reducing the acuity. Kreiker<sup>29</sup> attempted to dye the tarsal conjunctiva with gold chloride. While theoretically sound, the darkened lid allowing less light to reach the globe, the results were unsatisfactory. The dye brought about a serious inflammatory reaction, with consequent sloughing off of necrotic tissue and scarring. Furthermore, the dye disappeared from the area in several weeks. Ascher,<sup>30</sup> in 1930, suggested that, rather than the method of tattooing the periphery of the cornea, the wearing of contact lenses with an opaque sclera and iris might be effective. Müller of Wiesbaden made two experimental lenses, but there seems to be no report of any one actually trying to wear them. Streiff<sup>31</sup> made improvements on the Müller contact lenses and in 1 case, using one lens, found vision improved. Friede,<sup>32</sup> after attempting to dye both the conjunctiva and the sclera, obtained more satisfactory results in slitting the eyelids and implanting pigmented paraffin.

Great progress has been made in the past few years in the design and manufacture of contact lenses, and it was felt that a new attempt with a larger group of albinos was in order. Contact lenses have the advantage over lid pigmentation methods in that use of a smaller aperture, the size and shape of the pupil, is possible. Then, too, no surgical intervention is required. Since the lenses move with the eyes, nystagmus does not defeat their purpose, as it does for the pinhole goggles. The cosmetic effect of the contact lenses, if they are properly painted, can be extremely good.

Special sets of contact lenses with an opaque sclera and iris were made up for the group. It was hoped that they would enhance the vision of albinos, or at least give them greater comfort in high illumination. The test sets had a white sclera, a dark blue iris and a 3 mm. pupil. Of the 13 albinos who were willing to try the special lenses,

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29. Kreiker, A.: *Klin. Monatsbl. f. Augenh.* **77**:109-112 (Dec.) 1926.

30. Ascher, K. W.: *Klin. Monatsbl. f. Augenh.* **85**:829 (Dec.) 1930.

31. Streiff, J.: *Klin. Monatsbl. f. Augenh.* **89**:625-628 (Nov.) 1932.

32. Friede, R.: *Klin. Monatsbl. f. Augenh.* **77**:113-123 (Dec.) 1926; *ibid.* **85**:186-194 (Aug.) 1930; *Wien. med. Wchnschr.* **97**:159-160 (March) 1947.

12 were able to tolerate them (table 6). After the lenses were put on, each subject had refraction, standard test lenses being used. (Individual prescriptions can, of course, be ground in.) The acuity was then retested, using standard procedure, and the subject was afterward taken into bright daylight for his subjective feelings. Of the 12, 8 had their visual acuity enhanced over and above that with regular glasses—in 1 case from 10/200 to 10/70. The other 4 subjects had no measurable increase in acuity. The 8 with the enhanced acuity and 2 of the others felt much more comfortable in the high illumination and ceased to squint. The remaining 2 subjects (the oldest and the youngest) had no appre-

TABLE 6.—*Results with Special Contact Lenses\* on Vision in Albinos*

Subject	Tolerance	Visual Acuity	Strong Illumination
1.....	Good	RE: 10/70 LE: 10/70	Slight benefit
2.....	Not tolerated	.....	.....
3.....	Good	Same as with correction	Greater comfort
4.....	Good	Same as with correction	Greater comfort
5.....	Good	RE: 10/70 LE: 10/70	Greater comfort
6.....	Good	Same as with correction	Greater comfort
7.....	Good	Same as with correction	Greater comfort
8.....	Good	RE: 10/100 LE: 10/100	Greater comfort
9.....	Good	RE: 10/100 LE: 10/100	Greater comfort
10.....	.....	.....	.....
11.....	Good	RE: 10/70 LE: 10/70	Greater comfort
12.....	Good	RE: 10/70 LE: 10/70	Greater comfort
13.....	Good	RE: 10/70 LE: 10/70	Greater comfort
14.....	.....	.....	.....
15.....	Good	RE: 10/100 LE: 10/100	No benefit
16.....	.....	.....	.....

\* The contact lenses had an opaque white sclera and an opaque blue iris.

ciable increase in visual acuity or ocular comfort. It is felt that for the majority of albinos these special contact lenses would be of value.

#### SUMMARY

Complete albinism, a genetic recessive trait, is a relative lack of pigment. Ocular defects are always present. The lack of pigment causes the photophobia, while the amblyopia and nystagmus are due to the defective foveal region. Astigmatism and ametropia, while not directly related to the albinism, are correlated with it.

Albinism does not cause color blindness, although the poor acuity often results in low color discrimination. Form fields are likely to be somewhat contracted. Dark adaptation is fairly normal.

The simplest and most practical means of enhancing vision in albinos is probably through the use of contact lenses with opaque iris and sclera.

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# OPTIC NEUROENCEPHALOMYELOPATHY (DEVIC'S DISEASE)

## Report of a Case

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AND

LARRY L. CALKINS, M.D.

PHILADELPHIA

THE PURPOSE of this report is to present the clinical findings in a typical case of optic neuroencephalomyelopathy (neuromyelitis optica) with corroborative pathologic studies. This syndrome was first described by Allbutt<sup>1</sup> in 1870 but was so well summarized and analyzed by Devic<sup>2</sup> in 1894 that it is usually associated with his name. It consists of bilateral optic or retrobulbar neuritis and ascending myelitis manifested by paraplegia of the upper motor neuron type, which is commonly preceded by sensory disturbances. As pointed out in the standard textbooks of neurology and in a recent and excellent review of the literature by Silbermann,<sup>3</sup> this condition must be differentiated from the more acute encephalomyelitis arising spontaneously or after acute infections, from encephalitis periaxialis diffusa (Schilder's disease), which occurs in infancy and in childhood, and from the more chronic and relapsing multiple sclerosis.

Often called diffuse myelitis with optic neuritis, neuromyelitis optica, ophthalmoneuromyelitis or Devic's disease, it is defined pathologically as, "a form of subacute encephalo-myelitis characterized by massive demyelination of the optic nerves and spinal cord sometimes running a self limited and sometimes a progressive course."<sup>4</sup> The etiology is unknown.

## REPORT OF A CASE

J. L., a white man aged 45, was admitted to the ophthalmology service of the Hospital of the University of Pennsylvania on March 5, 1947, because of complete loss of vision. He first noted dimness of vision in both eyes on February 20, one week after a moderately severe, self-treated infection of the upper

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From the Department of Ophthalmology, Hospital of the University of Pennsylvania.

1. Allbutt, T. G.: On the Ophthalmoscopic Signs in Spinal Disease, *Lancet* 1:76, 1870.

2. Devic, M. E.: Myélite aiguë dorso-lombaire avec névrite optique, *Cong. franç. de med.* 1:434, 1894.

3. Silbermann, S. J.: Devic's Disease, *J. Nerv. & Ment. Dis.* 102:107, 1945.

4. Brain, W. R.: Diseases of the Nervous System, ed. 3, London, Oxford University Press, 1947.

respiratory tract. By February 25, on his admission to another hospital, he was totally blind. Ophthalmoscopic examination at that time revealed 2 D. of papilledema bilaterally, accompanied with numerous linear hemorrhages at the disk margins. A tentative diagnosis of intracranial neoplasm or cerebral abscess was made, and transfer was made to the Hospital of the University of Pennsylvania for further diagnostic facilities.

At the time of his admission to this hospital, throbbing frontal headache and numbness of the right leg had developed. He had no light perception in either eye. The lids, palpebral fissures and lacrimal apparatus were normal. Corneal sensitivity was not diminished. The pupils were semidilated and fixed to light. The left was slightly larger than the right. They constricted slightly on convergence and forced closure of the lids. Examination with the slit lamp showed minimal, senile, cortical cataractous changes in each lens.

Ophthalmoscopic examination showed clear media in each eye. The margin of each optic nerve head was blurred. Each disk was elevated 3 D., and there

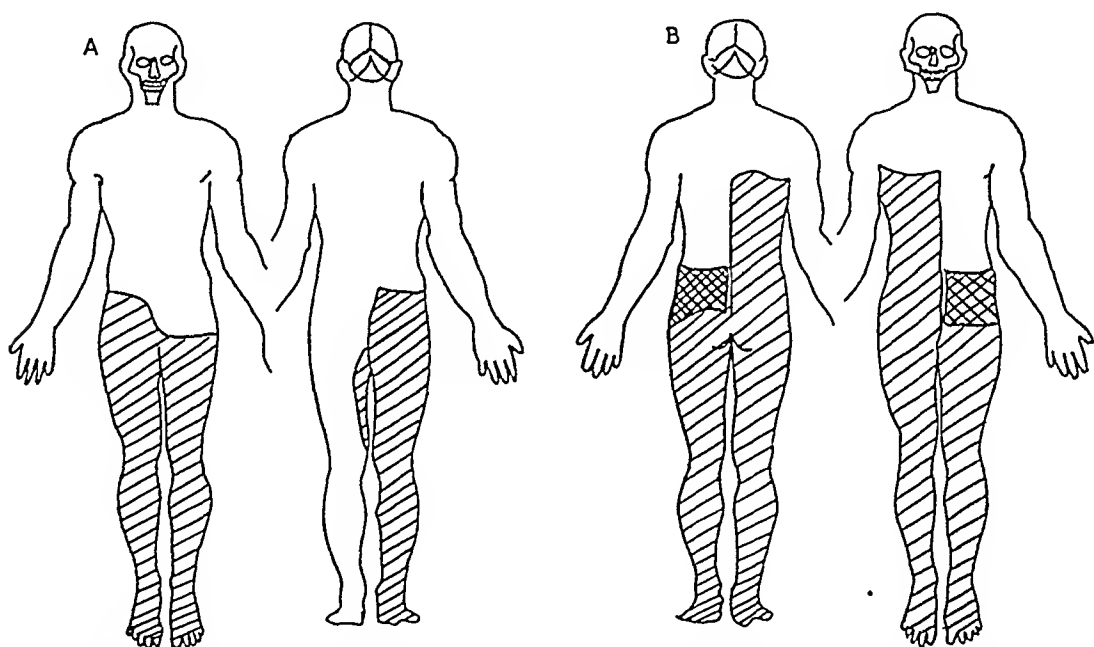


Fig. 1.—*A* (March 5, 1947), sensory loss to pinprick; *B* (March 9), sensory loss to touch, pain and temperature stimuli (single hatchure) and hyperesthesia to thermal stimuli (double hatchure).

was definite edema of the retina adjacent to the nerve head. Numerous hemorrhages and exudates were present on and near each optic nerve. The veins were moderately distended and slightly tortuous. The light reflexes of the retinal arteries were increased, and there were arteriovenous crossing defects near the disk.

Neurologic examination showed that all the cranial nerves except the second were intact. No pathologic reflexes were elicited. There was sensory loss to pinprick over both lower extremities, more pronounced on the right and extending to the crest of the ilium (fig. 1 *A*). The tentative diagnosis was optic neuro-encephalomyelopathy; other neurologic lesions had to be excluded.

The results of initial laboratory studies were normal, and on March 7, when motor weakness appeared in the lower extremities and the left arm, a lumbar puncture was performed under manometric control. The initial pressure was 70 mm. of water, and the cell count and protein estimation were within normal limits. Complete



roentgenographic examinations of the skull and chest revealed nothing abnormal. On March 9, the fourth day of hospitalization and the date of his transfer to the neurologic service, the patient exhibited increased motor disturbance and sensory loss. Deep touch, pain and temperature sensibility was lost below the sixth thoracic dermatome on the right and the first lumbar dermatome on the left. There was an area of hyperesthesia to cold on the left extending from the first lumbar to the ninth thoracic dermatome (fig. 1B). Difficulty in voiding, requiring catheterization, was noted at this time. A urethral stricture was found, and a catheter was left indwelling. By March 11, the Babinski sign was definitely positive on the left, and the temperature rose to 102 F., with spiking to 105 F. in eight hours. This elevation was thought to be urethral in origin. On March 13, eight days after his admission, some strength returned to the left arm and leg, and the patient was able to perceive bright light in the right eye. By March 15 he could tell the shapes of attendants, and two days later he could count fingers. On March 20 he was paralyzed in both legs and had severe abdominal distention. Within the next forty-eight hours, he had light perception in the left eye, and the sensory level was 3 cm. above the nipple line on the left and at the iliac crest on the right. On March 23, weakness in the arms was complete, and he first noted difficulty in swallowing. There was greater difficulty in breathing, and he was placed in a respirator. The force of cough was decreased, and a toothache type of pain, formerly present in the neck and arm, disappeared. Vision improved on the right so that objects were recognized. On March 27, he was unable to be out of the respirator; dulness of sensibility to pinpoint developed over the left side of the face, and he complained of deafness of the left ear. Vision continued to improve, and prompt pupillary reactions were present in both eyes. On March 28 he had a temporary episode of unconsciousness and a period of delirium, followed by death in a few hours, slightly more than five weeks after the onset of symptoms.

Cultures of the spinal fluid during the clinical course of the disease and of the spinal fluid and tissue of the central nervous system obtained at necropsy failed consistently to yield any pathogenic bacterium or virus.<sup>5</sup>

#### OPHTHALMOLOGIC AND NEUROPATHOLOGIC REPORT

*Gross Description.*—The right eye measured 24 by 23 by 23 mm. and appeared normal on transillumination. Oblique section revealed no abnormality. Cross section of the optic nerve revealed that the internal markings were indistinct. There was noticeable softening of the nerve, particularly just in front of the chiasm.

The left eye measured 24 by 24 by 22 mm. Transillumination revealed no shadow. Oblique section revealed nothing significant. Cross section of the left optic nerve resembled that of the right.

The brain showed widening of the sulci over the frontal lobe. The vessels of the surface were congested. The brain as a whole felt uniformly firm. The base of the brain, the brain stem and the cerebellum were normal in appearance.

In cross section the ventricles were of normal size and shape. There were oval and irregular areas of gelatinous softening in the white matter of the left parietal lobe. Gross section of the cerebellum showed nothing abnormal. The meninges were not grossly changed. The appearance of the spinal cord and the cauda equina was normal. Sections of the spinal cord showed some loss of normal configuration and disturbance of internal markings.

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5. Studies were carried out by Dr. Werner Henle in the bacteriology and virus laboratories of the Children's Hospital of Philadelphia.

*Microscopic Description.*—Pathologic material was fixed in dilute solution of formaldehyde U. S. P. (1:4) and was prepared in Müller's fluid as seemed indicated. All levels of the brain and spinal cord were studied with the standard hematoxylin and eosin stain. The general topographic pattern was followed in sections stained by the Weigert method. Cell aggregations were identified by the Nissl technic (toluidine blue). Some myelin degenerations were followed by treatment with osmium tetroxide, after the technic of Marchi. Silver staining was used as needed.

*Eyes:* Because of the meager knowledge of the nature of this disease, the eyes were not sent to the Eye Bank for Sight Restoration, but were submitted to pathologic examination.

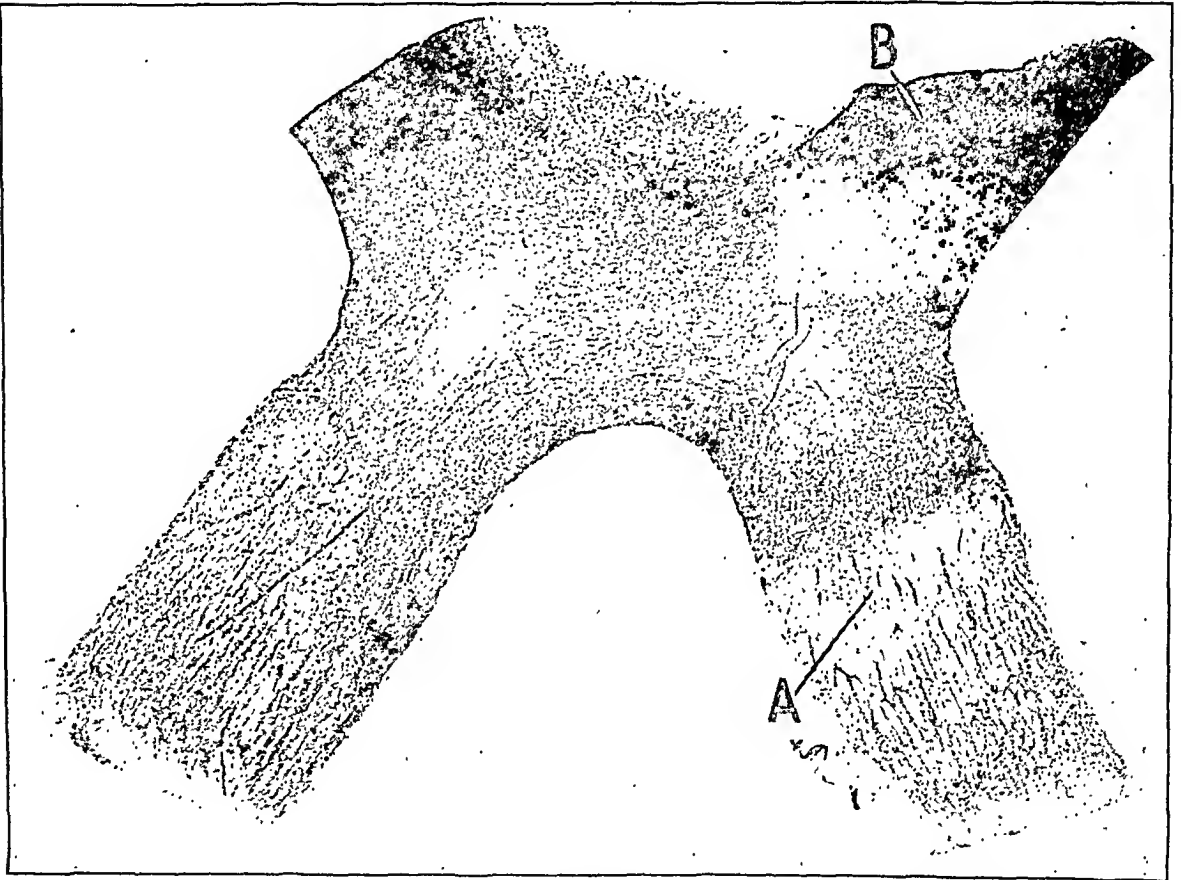


Fig. 2.—Optic chiasm showing demyelination of the optic nerves (A). The optic tracts are not involved (B).  $\times 8$ .

The changes in the right eye were limited primarily to the optic disk and nerve. The optic nerve showed almost complete demyelination to a point just proximal to the chiasm (fig. 2). Feeble glial proliferation was observed to be more pronounced nearer the eye. In the demyelinated areas compound granular corpuscles were seen, and variable amounts of lymphocytic infiltration occurred, occasionally showing accumulation about the central vessels. No hemorrhage was noted. In a small area just distal to the lamina cribrosa myelin sheathing was retained (fig. 3 A). The left eye was similar to the right except that there was less retention of myelin and status spongiosus occurred nearer the disk (fig. 4). Both disks showed minimal papillitis (fig. 3 B).

*Spinal Cord and Brain Stem:* Sections were taken from the cervical, mid-thoracic and lumbosacral areas.

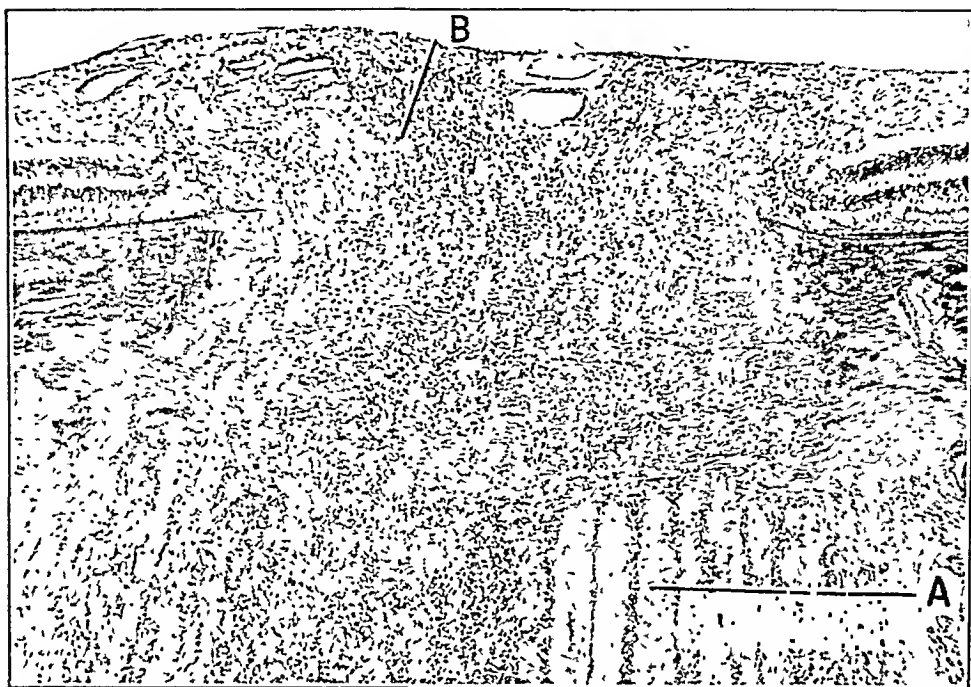


Fig. 3.—Section of the optic disk of the right eye, showing area of retained myelin (*A*),  $\times 80$ , and papillitis (*B*),  $\times 55$ .

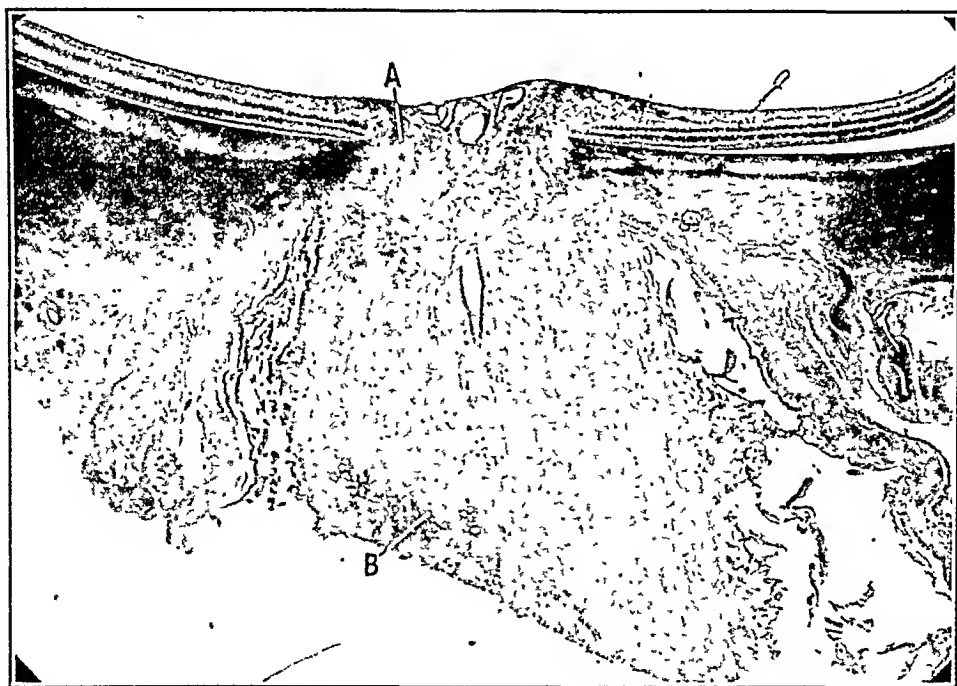


Fig. 4.—Section of the left optic nerve and disk, showing area of status spongiosus (*B*) and low grade papillitis (*A*).  $\times 16$ .



Fig. 5.—Section of the cervical portion of the spinal cord ( $\times 8$ ). Note particularly the changes around the periphery of the section.

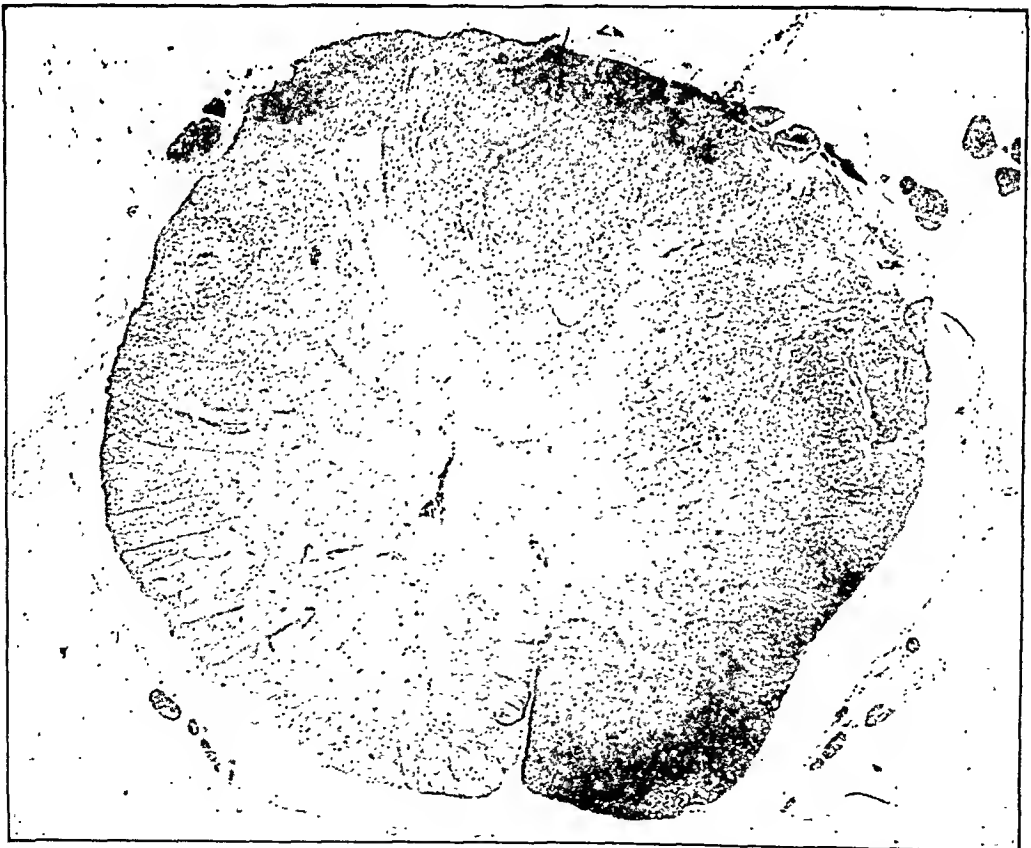


Fig. 6.—Section of the cervical portion of the spinal cord ( $\times 9$ ), showing an area of intense reaction where axis-cylinders are destroyed and cellular infiltration is most pronounced.

The lumbosacral sections showed diffuse demyelination of the posterior columns, with associated edema. There was no cellular activity in the area of demyelination, and the anterior horn cells stained normally.

Sections from the midthoracic region showed diffuse and irregular areas of demyelination, a major portion occurring around the periphery (fig. 5). One anterior column was more severely involved than the other. Status spongiosus was present in the areas of severe demyelination. Only occasional areas showed destruction of axis-cylinders, and here the cellular infiltration with lymphocytes was most intense. There was marked chromatolysis of the anterior horn cells. The meninges were not changed (fig. 6).

Sections through the high cervical portion of the cord and the lower portion of the medulla showed diffuse demyelination and areas of status spongiosus next to intact axis-cylinders and unchanged myelin sheaths. There was intense cellular

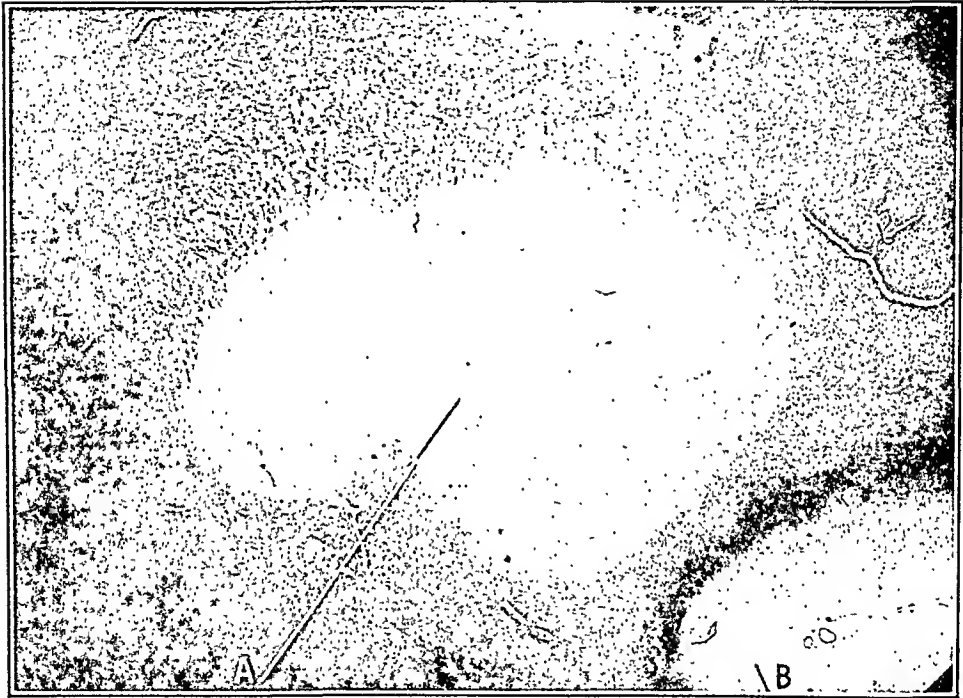


Fig. 7.—Section of the parietal cortex and subcortical white matter on the left side ( $\times 5$ ), showing focal area of demyelination (A) and cortex (B).

infiltration, consisting of lymphocytes and compound granular corpuscles. The anterior horn cells were only partly preserved. The meninges were not involved.

Sections through the medulla showed patchy areas of demyelination, the loss of myelin being mild and associated with simple edema. The ganglion cells were well preserved, and the meninges were spared.

Sections through the medulla in the area of the inferior olivary nuclei and the pons showed no change. Portions of the cerebellar cortex included in these sections appeared normal.

Sections of the diencephalon in the region of the anterior commissure showed sparing of this area.

**Cerebral Cortex:** Sections of the left parietal lobe (fig. 7) showed an irregular area of demyelination in the subcortical white matter; the lesion was well

delimited but was filled with many cells, most of which were compound granular corpuscles. Lymphocytes and plasma cells were occasionally seen. Coagulation necrosis was present centrally, and some of the surrounding blood vessels showed cuffs of lymphocytes. The meninges were not involved.

#### COMMENT

The profound temporary visual depression seen clinically in this case was correlated with severe demyelination in both optic nerves, the nearer the chiasm, the more pronounced the loss of myelin. This visual depression was thought to be secondary to the associated edema and toxemia from products of myelin degeneration. The failure to demonstrate interruption in the continuity of the axis-cylinders in severely damaged areas of the visual pathways is instructive in the light of the gradual return of vision in both eyes. The visual improvement was much more rapid after a period of hyperpyrexia of urethral origin, and there was an associated temporary lag in the ascent of the myelitis. The cervical portion of the cord in particular did show degeneration of axis-cylinders and anterior horn cells; this change was related to the clinical loss of many sensory modalities and the development of motor palsies.

The relatively afebrile clinical course and the feeble cellular response in the blood and the spinal fluid, as well as in sections of the central nervous system, are in accord with the experience of other investigators and are related to the failure to find a pathogenic bacterium or virus.

#### SUMMARY

A case of clinically typical optic neuroencephalomyelopathy (Devic's disease) is reported. Attempts to isolate an etiologic agent in this case were unsuccessful.

Pathologic studies showed demyelination of the optic nerves, the spinal cord and the subcortical white matter.

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## KERATOPLASTY IN TREATMENT OF KERATOCONUS

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**K**ERATOCONUS is a localized conus-shaped, or mound-shaped, noninflammatory ectasia of the central portion of the cornea. The protruding area generally extends over the central half of the cornea and is always thinner than normal, but in some instances the conus may be eccentric. In some cases the deformity, after beginning to develop, remains stationary, without tendency to become worse; this condition is designated as abortive keratoconus. In other cases it remains stationary after developing to a more advanced stage; the patient is still able to obtain fairly good vision with the aid of ordinary glasses, although this correction may require the use of high cylinders.

The cornea of the conus may be reduced to one fifth of its normal thickness and in extreme cases may become still thinner. Occasionally Descemet's membrane and its endothelial lining rupture, and the aqueous passes into the parenchyma of the cornea with the subsequent development of corneal edema or hydrops. When this occurs, the protrusion increases. The apex or the whole conus becomes turbid and the condition is made worse, until the endothelium regenerates and the acute ectasia clears up, either spontaneously or with the aid of pressure dressings, often with residual permanent scarring of the apex of the conus. In other cases of keratoconus there is gradual deterioration of the deformity, generally with progressive scarring of the apex, without the occurrence of acute edema. In some extreme cases the cornea is so thin that it perforates, either spontaneously or as a result of minor trauma, with the subsequent collapse of the anterior chamber.

Until the advent of the contact lens, patients with advanced keratoconus—who could no longer obtain useful vision with the use of ordinary glasses—had to remain in a nearly blind state or submit to surgical procedures.

### REVIEW OF THE LITERATURE

A review of the literature on the surgical treatment of keratoconus reveals a formidable number and variety of surgical procedures advocated for the alleviation of this disorder.

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Read at the Eighty-Fourth Annual Meeting of the American Ophthalmological Society, Hot Springs, Va., May 17, 1948.

The first surgical procedure for the cure of keratoconus was that of Ware,<sup>1</sup> who in 1810 advocated paracentesis of the anterior chamber, followed by moderate pressure to prevent the return of the protrusion. The same procedure was recommended by Dix<sup>2</sup> and Desmarres d'Evreaux<sup>3</sup> in 1847 and by Bell<sup>4</sup> in 1785. Adams<sup>1</sup> in 1817 advocated needling of the lens in order that the increased refractive error produced by the deformity of the cornea might be neutralized. Middlemore<sup>5</sup> in 1835 and Tyrell<sup>6</sup> in 1840 proposed moving the pupil from behind the most altered portion of the cornea. The operation consisted in incarcerating the iris in a corneal opening made near the limbus. In 1839 Favio<sup>7</sup> resorted to the removal of a V-shaped flap, at the apex of the cone, without the application of sutures. In 1858 Critchett<sup>2</sup> modified the operation of Middlemore and Tyrell by tying a single knot in the prolapsed iris with a fine silk thread. The strangulated portion of the iris fell off in about forty-eight hours, and the iris remained incarcerated in the corneal cicatrix. The procedure, named iridodesis by the author, left the pupil in the desired position for obtaining the most useful vision. Bowman<sup>8</sup> in 1859 resorted to the practice of double iridodesis. Having observed that vision in keratoconus improved frequently with the use of a stenopeic slit, he incarcerated the pupillary borders twice, near the limbus, at opposite ends of the same diameter. The result was the formation of a slitlike pupil which could be placed in any desired direction across the cornea; Bowman, however, expressed the belief that the vertically placed pupil was to be preferred. In 1866 von Graefe<sup>9</sup> recommended the dissection of the superficial layers of the cone with a knife, followed by the application of a silver nitrate stick for the purpose of producing a flattened scar after the ulcer was healed. Meyer<sup>10</sup> in 1887 also advocated von Graefe's operation, slightly modified. Bow-

1. Cited by Oliver, in Wood, C. A.: *A System of Ophthalmic Operations*, Chicago, Cleveland Press, 1911, vol. 2, p. 962.

2. Cited by Nance, in Wood, C. A.: *A System of Ophthalmic Operations*, Chicago, Cleveland Press, 1911, vol. 2, p. 1009.

3. Desmarres d'Evreaux, L. A., cited by Appelbaum,<sup>35</sup> p. 919.

4. Bell, B.: *A System of Surgery*, ed. 2, Edinburgh, Elliot, 1785, vol. 3, p. 325.

5. Middlemore: *A Treatise on the Diseases of the Eye and Its Appendages*, 1835, vol. 1, p. 538.

6. Tyrell: *A Practical Work on the Diseases of the Eye*, London, J. & A. Churchill, Ltd., 1840.

7. Cited by Oliver, in Wood, C. A.: *A System of Ophthalmic Operations*, Chicago, Cleveland Press, 1911, vol. 2, p. 963.

8. Bowman, W.: *Roy. London Ophth. Hosp. Rep.* **2**:154, 1859-1860.

9. von Graefe, A.: *Arch. f. Ophth.* **4**:271, 1858.

10. Meyer, E.: *Diseases of the Eye*, Philadelphia, P. Blakiston & Sons Company, 1887, p. 149.



man <sup>11</sup> in 1869 and in 1873 resorted to the trephining in removing the superficial layers of the corneal cone. The center of the bulged area thus dissected was punctured and kept open with repeated paracenteses until the cone had flattened. In 1872 Bader <sup>7</sup> claimed to have obtained favorable results by excision of an elliptic piece of full corneal thickness at the apex of the cone. To reduce the danger of prolapse of the iris in Bader's operation and to assist in early closure of the wound, Badal <sup>12</sup> in 1901 inserted three horsehair sutures vertically through the cornea prior to the removal of the apex. The sutures were quickly tied after excision of the elliptic piece of cornea. Critchett <sup>13</sup> in 1895 also advocated the removal of a small elliptic piece of the cone at the apex. The incision was begun with a knife and completed with scissors. Wolfe <sup>14</sup> in 1882 first produced an opacity of the apex of the cone and then made a small artificial pupil behind a transparent cornea. Grandclement <sup>15</sup> in 1891 advocated tattooing of the cone and optical iridectomy. In 1905 Stoewer <sup>15</sup> used a conjunctival flap to cover the cornea after the excision of the cone.

The cautery was used in the treatment of keratoconus as early as 1879 by Gayet <sup>16</sup> and by Andrew <sup>17</sup> in 1884 and by Critchett <sup>18</sup> in 1895. Since then, the number of contributions endorsing the use of the cautery has been immense. Among the many authors recommending cauterization of the apex of the cone are Tweedy <sup>19</sup> and Sattler <sup>20</sup> in 1900; Swanzy, <sup>21</sup> in 1903; Siegrist, <sup>22</sup> in 1916, and Knapp, <sup>23</sup> in 1929. Siegrist recommended cauterization combined with repeated paracente-

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11. Bowman, W.: *Observations on Various Practical Points of Ophthalmology*, Report of Fourth International Ophthalmological Congress, Savill Edwards & Company, 1873, pp. 177-183; footnote 10.

12. Badal: *Arch. d'opht.* **21**:433, 1901.

13. Cited by Oliver, in Wood, C. A.: *A System of Ophthalmic Operations*, Chicago, Cleveland Press, 1911, vol. 2, p. 969.

14. Wolfe, J. R.: *On Diseases and Injuries of the Eye*, Philadelphia, P. Blakiston & Sons Company, 1882, p. 85.

15. Stoewer, W.: *Klin. Monatsbl. f. Augenh.* **43**:474, 1905.

16. Gayet, cited by Oliver, in Wood, C. A.: *A System of Ophthalmic Operations*, Chicago, Cleveland Press, 1911, vol. 2, p. 968.

17. Andrew: *Brit. M. J.* **2**:903, 1884.

18. Critchett, cited by Nance, in Wood, C. A.: *A System of Ophthalmic Operations*, Chicago, Cleveland Press, 1911, vol. 2, p. 1010.

19. Tweedy, cited by Nuel, Norris and Oliver, *System of Diseases of the Eye*, Philadelphia, J. B. Lippincott & Company, 1900, vol. 4, p. 252.

20. Cited by Oliver, in Wood, C. A.: *A System of Ophthalmic Operations*, Chicago, Cleveland Press, 1911, vol. 2, p. 971.

21. Swanzy, H. R.: *A Handbook of Diseases of the Eye and Their Treatment*, Philadelphia, P. Blakiston & Sons Company, 1903.

22. Siegrist, A.: *Klin. Monatsbl. f. Augenh.* **56**:400, 1916.

23. Knapp, A.: *Keratoconus: Etiology and Treatment*, *Arch. Opth.* **2**:658 (Dec.) 1929.

ses. Swanzy stated that cauterization should not produce perforation of the cornea, whereas Tweedy and Knapp were supporters of perforation. Elschmig<sup>20</sup> in 1904 superficially cauterized the apex of the cone, as well as an area of the same width connecting the apex with the nearest point of the conjunctiva at the limbus, the object being to produce vascularization with subsequent proliferation of the connective tissue and flattening of the cone. Keratoconus was cured by Carpenter<sup>24</sup> in 1915 with the use of the high frequency spark. Iridectomy was used by von Graefe<sup>25</sup> in 1858 and was advocated by Wells<sup>26</sup> in 1869. Corneoscleral fistulization was recommended by Adams<sup>27</sup> and Tiffany<sup>28</sup> in 1914, by Green<sup>29</sup> in 1920 and by Wibo<sup>30</sup> and Rasquin<sup>31</sup> in 1934. Fox<sup>32</sup> reported in 1925 that flattening of the cone may follow excision of a corneal segment adjacent to the ectatic portion.

Extraction of the lens, which was advocated by Adams<sup>1</sup> in 1817, was employed by Nicolato,<sup>33</sup> in 1930; the latter recommended extraction of the lens in adults and repeated discissions in younger patients.

Sato<sup>34</sup> in 1941 advocated the splitting of Descemet's membrane in an effort to flatten the cornea.

The technics just enumerated are of three types: (1) intraocular operations, (2) excision of a portion of the cornea and (3) flattening of the cornea by cauterization or other means.

The advocates of the first type, intraocular operations, such as paracentesis, extractions of the lens, deviation of the pupil and fistulization, aim to neutralize the corneal deformity with intraocular alterations; but they leave the corneal deformity, with the real cause of poor vision, unchanged.

Advocates of the second type, recommending corneal excision, approach the problem more sensibly because they try to cure or improve the condition by the removal of the deformity in order to obtain a more normal corneal curvature. This type of surgical treatment, however, is too often disastrous to the eye. The operation frequently results in complications, such as high astigmatism, adherent leukoma, often

24. Carpenter, E. R.: *Ophth. Rec.* **24**:18, 1915.

25. von Graefe, A.: *Arch. f. Ophth.* **12**:215, 1866.

26. Wells, J. S.: *A Treatise on the Diseases of the Eye*, Philadelphia, Henry C. Lea, 1869, p. 142.

27. Adams, P. H.: *Ophthalmoscope* **12**:132, 1914.

28. Tiffany, F. B.: *Ophth. Rec.* **23**:379, 1914.

29. Green: *Am. J. Ophth.* **3**:459, 1920.

30. Wibo, M.: *Bull. Soc. belge d'opht.* **68**:90, 1934.

31. Rasquin, M.: *Bull. Soc. belge d'opht.* **69**:11, 1934; abstracted, *Am. J. Ophth.* **18**:789, 1935.

32. Fox, L. W.: *Tr. Ophth. Soc. United Kingdom* **45**:92, 1925.

33. Nicolato, A.: *Arch. di ottal.* **37**:74, 1930.

34. Sato, T.: *Klin. Monatsbl. f. Augenh.* **107**:234, 1941.

extending to the pupillary area, and secondary glaucoma. Therefore these technics have been considered unsatisfactory, and hence have never become popular.

By far the most successful, and the least likely to cause serious intra-ocular complications, have been the procedures of the third type, for the purpose of flattening the conus by scar tissue formation—whether the scar is brought about by cauterization of the conus with chemicals, electrocautery, high frequency current or the splitting of Descemet's membrane. These surgical procedures result in temporary or permanent improvement of vision, although this improvement seldom approaches vision within normal limits. Furthermore, the scarring designed to flatten the cornea not infrequently defeats the purpose of the operation by leaving the eye with no improvement in vision or with worse vision than before, in addition to corneal opacities which are undesirable from the cosmetic standpoint.

Appelbaum<sup>35</sup> in 1936 published an excellent paper discussing in detail the etiology, pathologic characteristics, symptomatology, objective signs and medical, optical and surgical treatment of keratoconus. Concerning the surgical treatment of this disease, Appelbaum stated:

Surgical intervention aims to produce flattening of the cornea in order to improve eyesight. When any degree of useful vision is no longer obtainable with the use of contact glasses, operative intervention may be considered—but not sooner. Only in cases of advanced, or nearly hopeless conditions should the patient undergo operation. Most ophthalmologists agree with this. Too much cannot be expected of surgical treatment; at best, it gives a result far from ideal and none too lasting. The unsightliness which inevitably follows must be anticipated, and the appearance of the eye is always marred to some extent.

Afterward, summarizing his discussion on the surgical treatment of keratoconus, Appelbaum stated:

Finally, in stating an opinion concerning the merits of the operations proposed by an equal number of competent surgeons, one could not improve, even today, on the statement of Wells, in 1873: "All these methods of treatment of conical cornea are still upon their trial and nothing decisive can as yet be said as to their relative advantages and disadvantages."

Entirely agreeing with the statements of Appelbaum and Wells,<sup>36</sup> I was convinced that the choice of a surgical method for the treatment of advanced keratoconus could not be made from the methods previously described. An impartial evaluation of their efficacy proved that more often than not they brought about a deterioration of the eye instead of the improvement they were supposed to accomplish. I also felt that

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35. Appelbaum, A.: Keratoconus, *Arch. Ophth.* 15:900 (May) 1936.

36. Wells, J. S.: *A Treatise on the Diseases of the Eye*, ed. 2, London, J. & A. Churchill, Ltd., 1873, p. 145.

only patients whose condition is considered hopeless—whose vision cannot be improved by the use of ordinary lenses or contact lenses, or who cannot tolerate contact lenses—should be subjected to operation.

The advent of contact lenses enabled many sufferers from keratoconus whose vision could not be improved with ordinary glasses to obtain useful vision; but there are still many whose vision, on account of dense scarring at the apex, cannot be improved with the use of contact lenses. There are others who with the aid of contact lenses have restoration of fairly good vision, but, who, owing to ever increasing irritation, do not tolerate the contact lenses well. In still another group of patients, contact lenses are not satisfactory because of their tendency to cause cloudiness of the cornea or because the buffer solution becomes turbid too rapidly. For all these patients with advanced keratoconus, with very precarious vision—less than 20/200 (industrial blindness)—whose vision does not improve with ordinary or with contact lenses or who do not tolerate the contact lenses well surgical intervention is justified.

#### REQUIREMENTS IN SURGICAL TREATMENT OF KERATOCONUS

In the successful treatment of keratoconus two requirements must be observed: 1. Since poor vision seems to be caused by the corneal deformity alone, and not by other intraocular pathologic conditions, surgical procedures must be limited to the cornea.

In order to obtain the best possible vision, the whole corneal protrusion must be removed and replaced with corneal tissue of normal curvature and thickness. The pupillary area must be free of scarring.

The only surgical procedure which fulfils these two requirements is keratoplasty of the partial penetrating type. Therefore, keratoplasty seems to me the logical procedure in advanced cases of keratoconus when useful vision can no longer be obtained with the use of ordinary or contact lenses or when contact lenses are not well tolerated.

In 1936 I<sup>37</sup> performed the first keratoplasty in a case of advanced keratoconus, with resulting pronounced improvement of vision and seemingly lasting cure. Encouraged by the first trials, I proceeded to treat other patients with advanced keratoconus with corneal transplantation. The results have been most encouraging. A high percentage of patients remain with clear grafts, marked improvement of vision and, so far as my twelve years' experience indicates, permanent cure. I have already operated on more than 200 persons with advanced keratoconus, and in more than 80 per cent the results can be considered most successful. The average improvement of vision that can be expected is from 20/200 or less to 20/50 or better (figs. 1 and 2).

37. Castroviejo, R.: *Internat. Abstr. Surg.* 65:5, 1937.

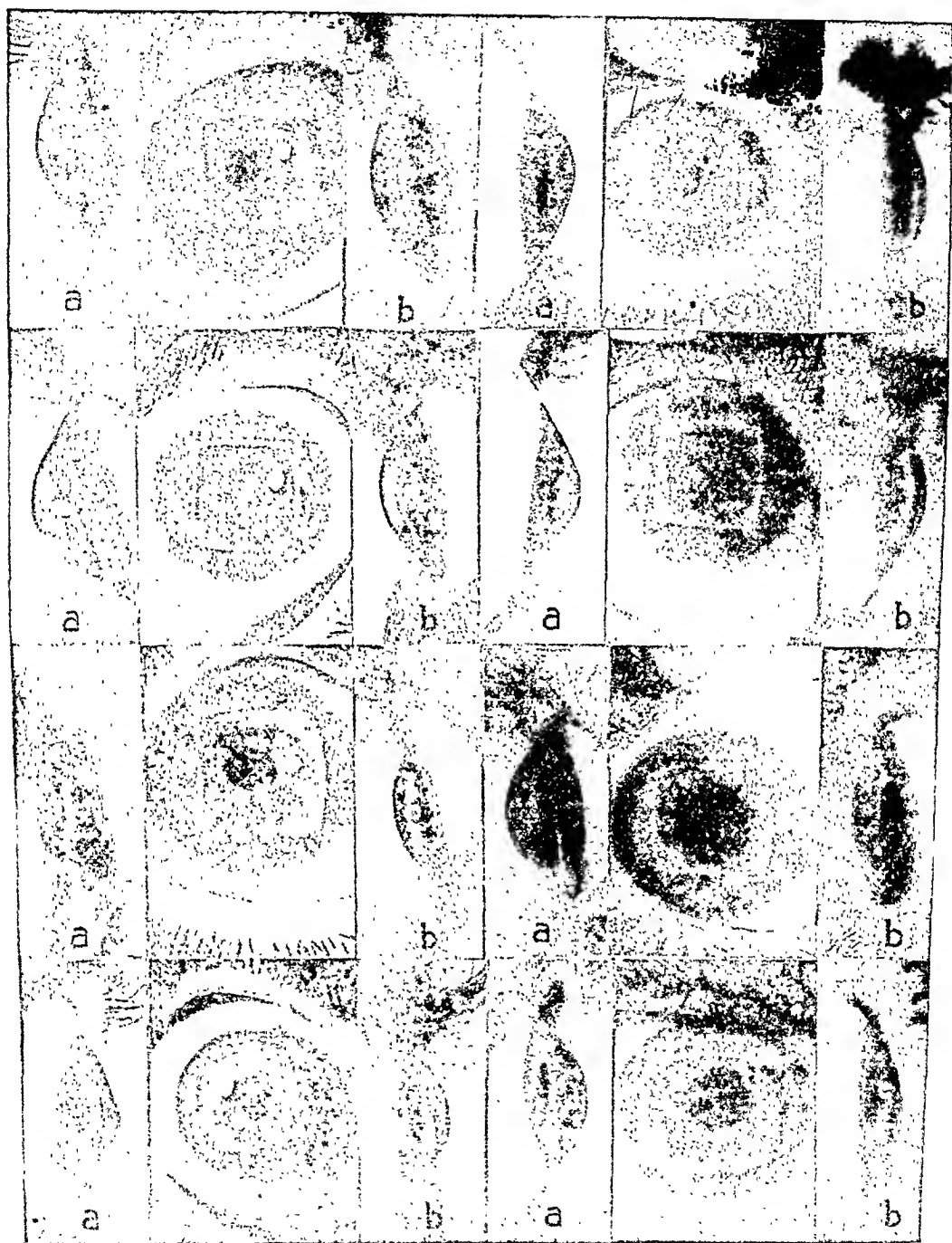


Fig. 1.—Clear square corneal transplants in eyes with advanced keratoconus. Profiles show the cornea (a) before operation and (b) after operation.

I have singled out keratoconus for this discussion on keratoplasty because keratoconus has special features which distinguish it from other corneal opacities or deformities. Failure to observe certain rules in the treatment of keratoconus by keratoplasty may defeat the success of the operation. The rules concerning these special features must be taken into consideration during the preoperative study, at the time of the operation and during postoperative recovery.

#### PREOPERATIVE STUDY

During the preoperative study, the thickness of the cornea and the extent of the keratoconus must be carefully studied with the slit lamp and the corneal microscope. It is important to know how extensive the keratoconus is, because the size of the graft and its location depend on the extent and location of the conus. The graft must be large enough to substitute for all, or as much as possible, of the conus. If the transplant is smaller than the conus, the deformity is likely to progress. The graft will not form a keratoconus, but the remaining thin cornea will

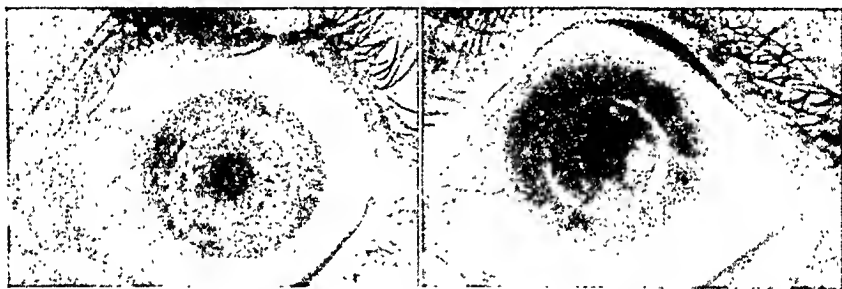


Fig. 2.—Clear circular transplants in eyes, with advanced keratoconus.

continue to protrude; or, if it does not advance after the operation, the graft, although clear, remains set in a protruding area of cornea, which results in very high myopia or astigmatism or both, thus defeating the visual purpose of the operation.

The patient shown in figure 3 serves to illustrate this point. He had advanced keratoconus in both eyes; vision in each eye was equal to counting fingers at 1 foot (30 cm.), and, on account of the pronounced conus, he could not be fitted with comfortable contact lenses. A corneal transplantation was performed on the right eye, using a 4.5 mm. graft (fig. 3 *a*). The transplant remained clear but was set in a protruding area, which resulted in very high myopia and astigmatism. Vision improved only slightly after the operation because of the remaining protrusion. In the fellow eye, a keratoplasty was performed afterward, using a transplant of 5.5 mm. (fig. 3 *b*). Again, this transplant was found to be too small; thin cornea remained, with subsequent protrusion of the graft and only slight improvement in vision. A third transplant, of 6 mm., was then used (fig. 3 *d*), the second on the left eye. but

still it was not large enough to permit excision of the whole conus. The result was moderate protrusion and high myopia of  $-20$  D. Corrected vision was 20/50. Finally, the right eye was again operated on, and, with the experience of three previous operations, a larger transplant of 7 mm. (fig. 3 c) was used, by means of which the whole conus was excised. Fairly good corneal curvature was obtained, and with a correction of  $-4.00$  sph.  $\ominus -1.75$  cyl., axis 120 vision was 20/25—3.

The smallest graft to be used in correction of keratoconus should be 6 mm., except in some cases of an extremely small conus. In such instances grafts of 5.5 mm., or even less, can be used. In cases of more pronounced keratoconus, grafts of 6.5 mm., or as large as 7 mm., are necessary.

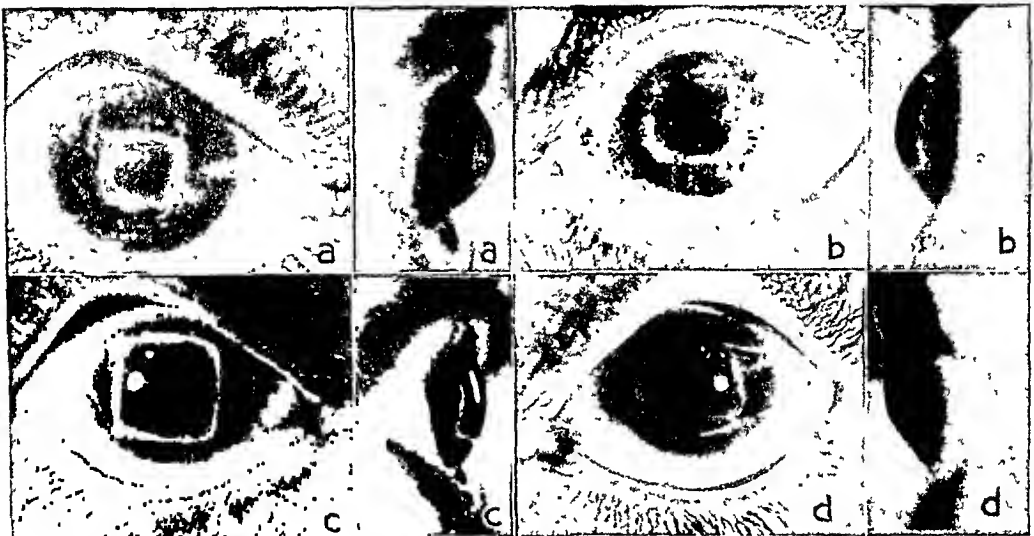


Fig. 3.—Four corneal transplantations performed on the two eyes of the same patient: (a) 4.5 mm. graft; (b) 5.5 mm. graft; (c) 7 mm. graft; (d) 6 mm. graft.

It is always desirable to place the graft in the center of the cornea in order that the center of the graft will coincide with the center of the pupil. In cases of keratoconus, however, the location of the graft must be controlled to a certain extent by the location of the conus. When the conus is off center, the graft should be displaced accordingly, in order to remove as much as possible of the protruding area. In this case, if the graft is small (less than 6 mm.), its edge may fall in or near the pupillary area, interfering with vision. This interference is, of course, greater if the cicatrix is made more pronounced during the healing process, thus reducing the useful area of the graft falling within the pupillary area (fig. 4B). If the graft is large (6 mm. or more), even in case of abundant scarring at the edges there is always enough useful area of the graft in the pupillary area.

This useful area for the same size of graft is larger in the square graft than in the circular one if the corners are placed as illustrated in figure 4 *A*. This fact should make the square graft more desirable than the circular one in a case of large keratoconus. In addition, the corners in the square graft extend farther toward the limbus, and

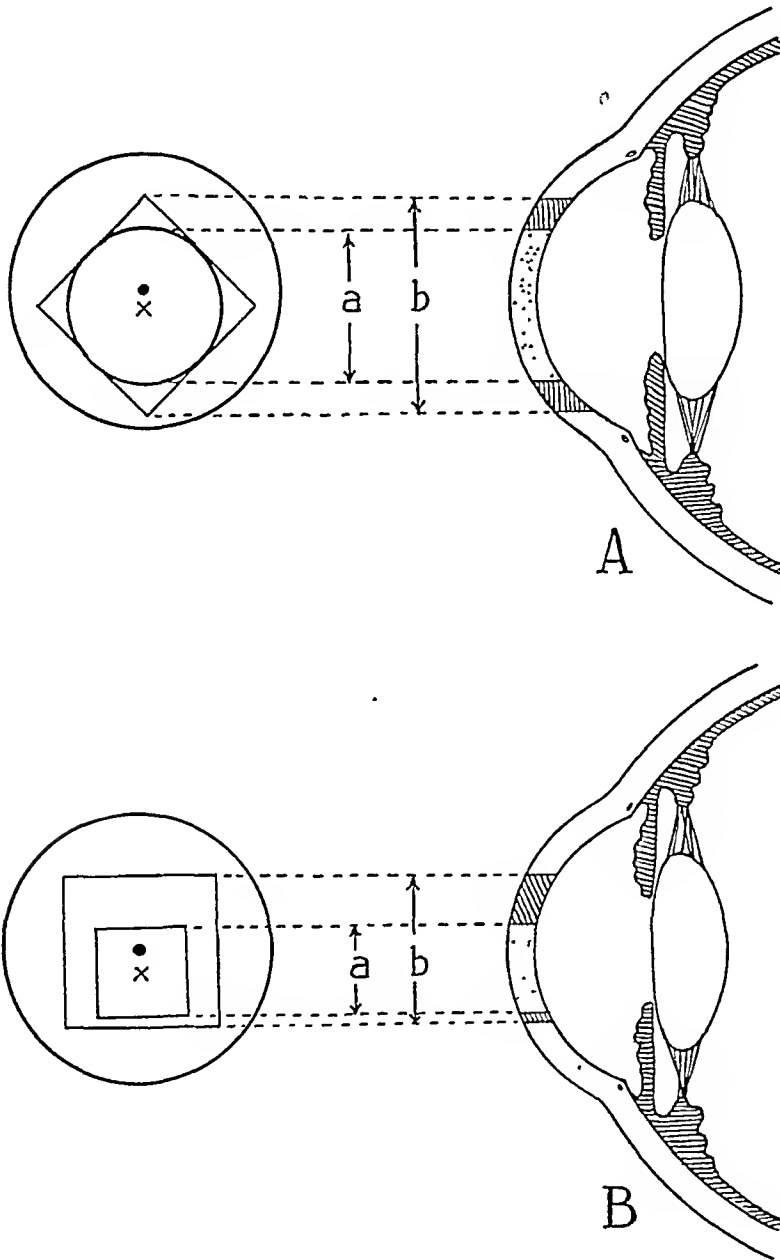


Fig. 4.—Diagrams showing (*A*) the position of the edges of eccentrically placed round (*a*) and square (*b*) grafts in relation to the pupillary area (the dot shows the center of the cornea, while the cross shows the center of the graft); (*B*) the position of the edges of the eccentrically placed small graft (*a*) and larger graft (*b*).

the scarring which takes place at the incision has a tendency to greater flattening of the graft and the cornea of the host, resulting in better curvature, than when a round graft is used. In order to accomplish the



same effect, a round graft would have to be much larger, corresponding to the distance, not from opposite sides of the square graft, but from corner to corner (fig. 5).

Another factor which must be considered before operation is the dilation of the pupil. When large grafts are used, the pupil should be widely dilated to prevent the formation of anterior synechia, one of the most frequent complications in keratoconus. The pupil generally dilates widely with repeated instillations of 3 per cent solution of atropine sulfate and 10 per cent emulsion of phenylephrine (neo-synephrine®) hydrochloride. If the pupil should fail to dilate beyond the limits of the area where the graft will be located in the cornea, it is preferable to use a smaller graft or to prepare the eye with a large iridectomy rather than

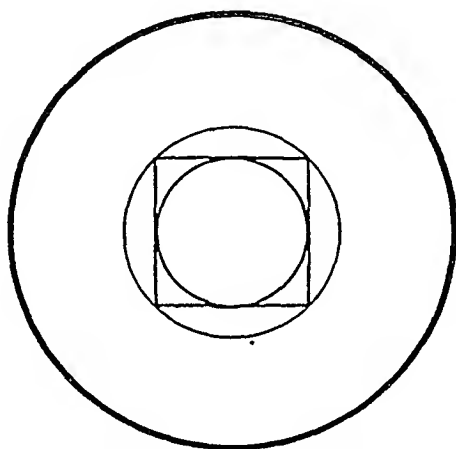


Fig. 5.—Diagram showing the relation of useful vision for grafts of the same size in the square and in the round transplant.

risk the development of anterior synechia, with subsequent danger of opacification of the graft or secondary glaucoma or both.

In addition to these local factors in the eye, the general condition of the patient should be carefully studied, eliminating all pathologic conditions which are likely to influence the normal postoperative course of the transplant, such as foci of infection, malnutrition and other systemic conditions. Infections in the nose and throat are particularly likely to cause postoperative uveitis, and it would be advisable not to perform a corneal transplantation in the presence of infected tonsils or pathologic conditions of the nose, including involvement of the sinuses, but to delay the operation until these conditions have been cleared up by medical or surgical treatment.

The two types of operation performed in this series have been the square and circular partial penetrating keratoplasties, illustrated in

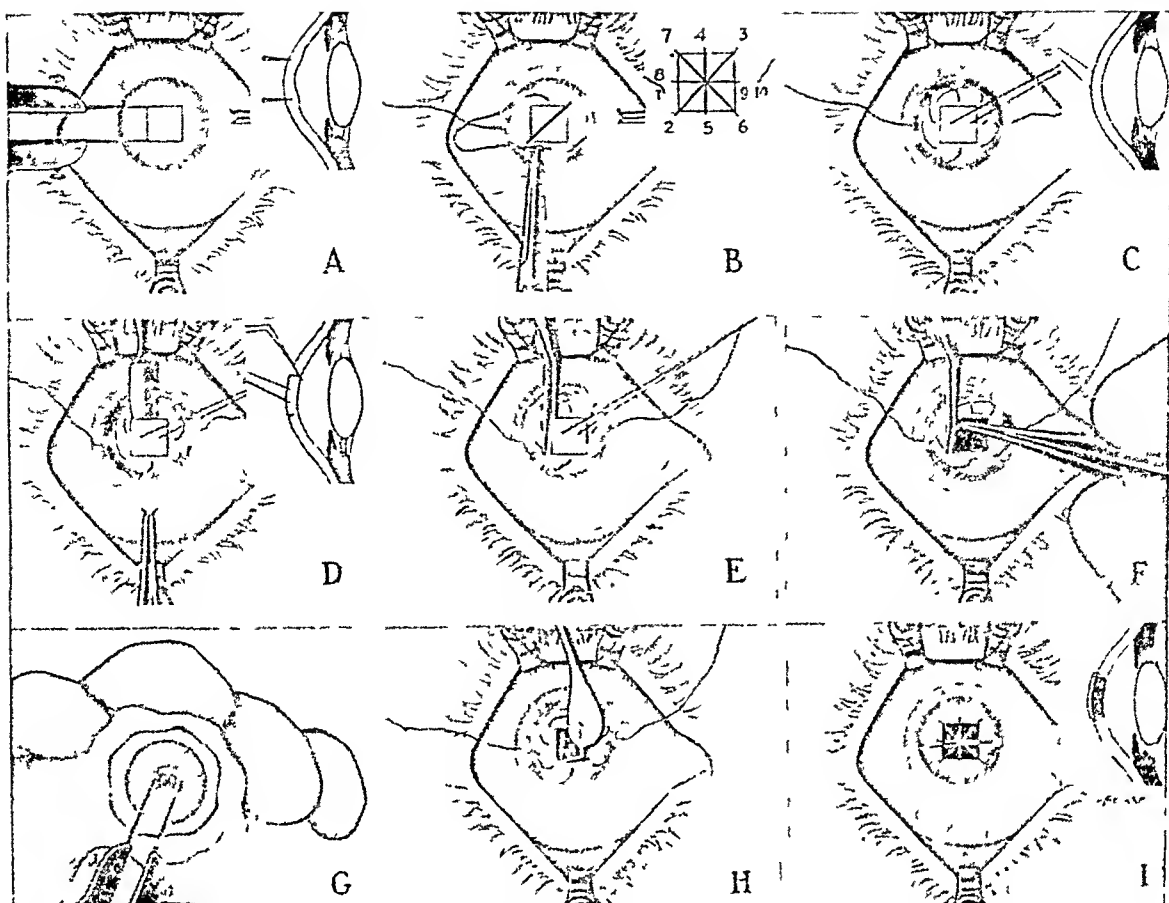


Fig. 6.—Successive steps in the Castroviejo square partial penetrating keratoplasty.

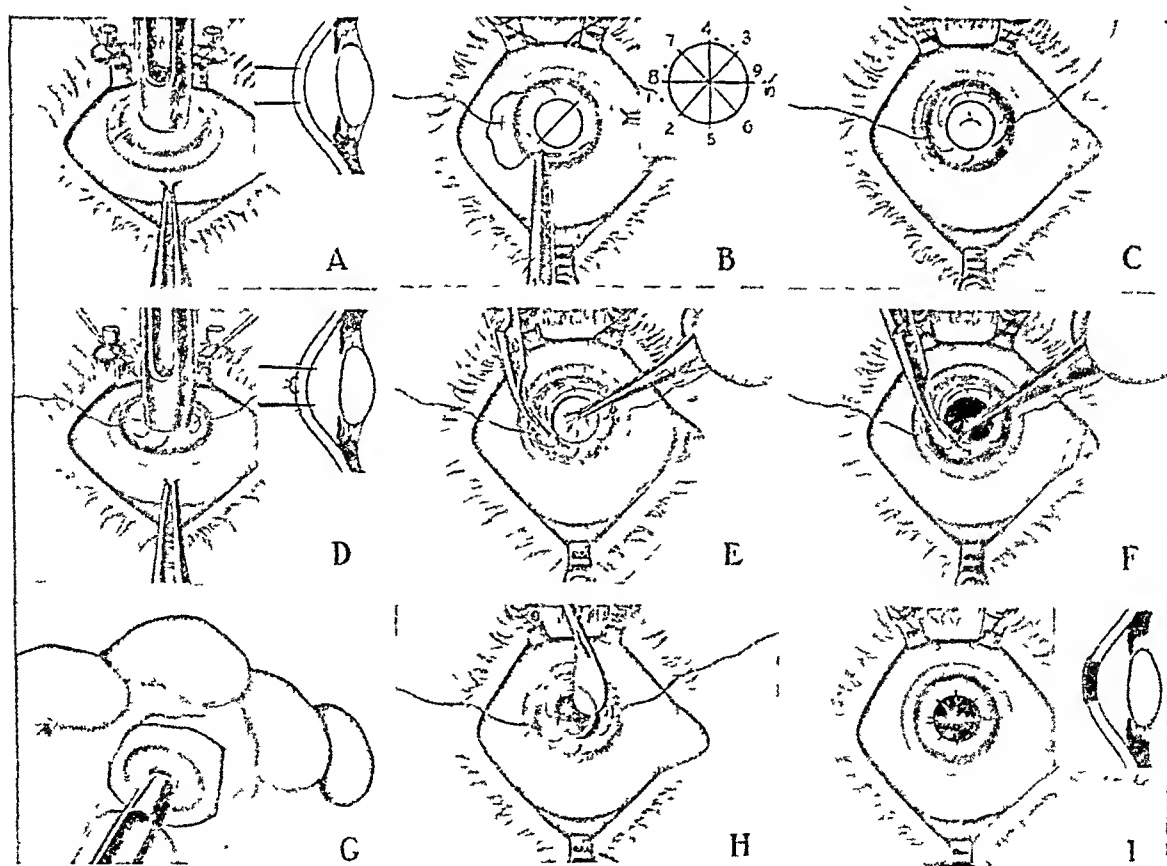


Fig. 7.—Successive steps in the Castroviejo circular partial penetrating keratoplasty.

figures 6 and 7. A detailed description of the operation has been given in another article.<sup>38</sup>

#### THE OPERATION

It has already been mentioned that the cornea of the conus is sometimes reduced to one-fifth the normal thickness and that in extreme cases it may be still thinner. On account of this thinness, the cornea may be perforated while the incisions are being outlined or the sutures are inserted. If the perforation occurs while the incisions are being outlined, whether with the double-bladed knife or with the trephine, before the sutures have been inserted, it may be difficult to continue the operation. However, the surgeon well trained in keratoplasty will be able, although with more difficulty, to continue with the operation and to place the sutures after the cornea has been perforated, particularly if the suture material is good. In this event, the remaining (uncut) portion of the incision must be completed with the aid of scissors, both in the square and in the circular graft. For the surgeon less skilled in this type of operation, it would be preferable to postpone the operation for about a week, to provide time for the cornea to close the opening firmly and the anterior chamber to reform, before proceeding with the operation.

If the perforation of the cornea takes place while the sutures are being inserted, because the anterior chamber has been entered with the needle, the aqueous humor will drain slowly, rendering the eye hypotonic. If this complication takes place in eyes with normal corneal thickness, it is feasible—and not difficult—to withdraw the needle and pass it through more superficial layers of the cornea; otherwise, a fistula may form during postoperative recovery, with drainage of aqueous humor, flattening of the anterior chamber and likelihood of intraocular infection, development of anterior synechia and secondary glaucoma.

In the area of keratoconus, it is possible to carry out the same maneuver of withdrawing the needle and passing it through more superficial layers of the cornea; but, because of the extreme thinness of the cornea in some cases and its lack of rigidity and resiliency, the cornea collapses and wrinkles (fig. 8 *A* and 8 *B*), so that the reinsertion of the needle may be extremely difficult. In these circumstances, also, the surgeon well trained in keratoplasty may proceed with the operation to a successful conclusion; for the less skilled surgeon, however, it would be preferable to postpone the surgical procedure rather than risk failure in the operation.

After the removal of the conus, particularly in eyes in which a large transplant of 6.5 mm. or more is used, the pupil may be found to be without sufficient dilatation and the size of the pupil to be smaller than

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38. Castroviejo, R.: *Am. J. Ophth.* 24:1 (Jan.); 139 (Feb.) 1941.

the opening in the cornea. This situation can be prevented before the operation, as has already been noted, by repeated instillations of 3 per cent atropine sulfate and 10 per cent emulsion of phenylephrine hydrochloride and, at the time of the operation, by injection under the conjunctiva of 2 per cent cocaine and a solution of epinephrine hydrochloride (1:1,000). If, in spite of this preparation before the graft is placed in position, the pupil is smaller than the opening in the cornea, direct instillation of 4 per cent cocaine and solution of epinephrine hydrochloride (1:1,000 or even 1:100) into the corneal opening may dilate the pupil wider than the corneal window. If, in spite of the instillations,

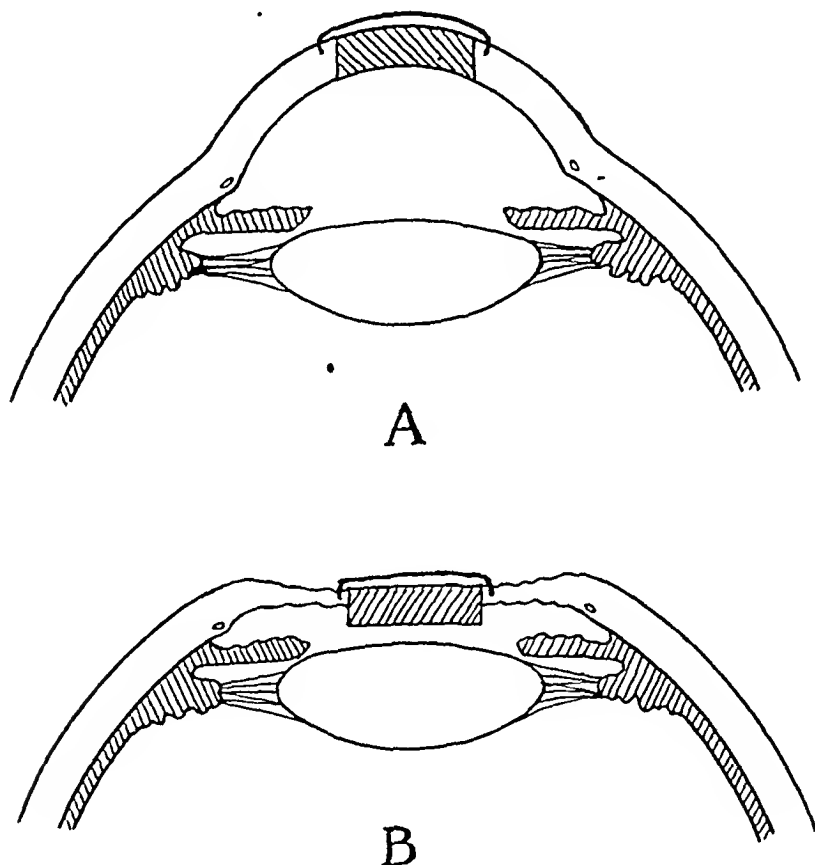


Fig. 8.—Diagrams showing (A) resilient cornea holding the graft in position and (B) collapsed and wrinkled thin cornea held in position around the graft by sutures placed close to the borders.

the iris shows within the opening, it is advisable to excise the involved portion of iris and place sutures from border to border, as illustrated in figure 9, a procedure which, although injuring the graft somewhat, gives a better coaptation of the borders, promoting early restoration of the anterior chamber and tending to avoid the development of anterior synechia. The performance of an iridectomy in these cases will, of course, be contested by those who perform keratoplasty with contracted pupil. Statistics will show in the future which method gives the greater number of anterior synechias—the one using the contracted pupil or

the one using the dilated pupil. Both my experimental work on animals and my clinical experience have proved to me that when the pupil is left contracted at the time of placing of the graft, anterior synechia is more likely to develop.

Because of the lack of resiliency of the cornea and the large grafts generally used in cases of advanced keratoconus, it is easier to injure the lens while perforating the cornea than while operating on eyes with normal corneal thickness and resiliency, in which smaller grafts are usually used. Therefore, in making the corneal perforation, particularly with the trephine, great care must be exercised to withdraw the trephine quickly, immediately after penetration into the anterior chamber has taken place, because the cornea collapses and the lens capsule comes into contact with the edge of the trephine almost instantly. Because of the large area of lens exposed when the graft is large, the lens is more easily injured while the border of the incision is being trimmed, if that should be necessary. Therefore, the extreme care that must be exercised during these manipulations to avoid injury to the lens cannot be emphasized too strongly.

I wish to mention another complication that may occur in cases of advanced keratoconus. In 1 instance I used a square transplant of 7 mm. to replace completely the extensive area of extremely thin cornea of the keratoconus. After the conus was excised, without injury to the lens, the lens mushroomed through the corneal opening and spontaneously extruded itself intact in its capsule. In this case, in order to maintain the graft firmly in position, it was necessary to suture the border of the graft to the border of the cornea of the host, using eight sutures, in the manner illustrated in figure 9.

If the lens is injured by the keratome or trephine or scissors while one is completing the incision, it is advisable to remove as much as possible of the injured lens, including the capsule. In this complication, the vitreous has a tendency to prolapse during the operation or the postoperative recovery, and thus to dislocate the graft. Therefore, it is advisable in these cases, in order to maintain the graft firmly in position, to suture the graft to the cornea of the host, border to border, as illustrated in figure 9.

In the case of large grafts, it is advisable to have the graft ready before the excision of the cornea of the host, in order not to delay the closing of the corneal opening as soon as the dissection of the conus has been concluded.

In corneas with keratoconus, contrary to what occurs in corneas with normal thickness and resiliency, there is a tendency for the cornea to collapse. This often results in an opening of the host cornea smaller than the graft, although the graft had been made the same size as the corneal opening. In this case, contrary to what happens with corneas

of normal thickness and normal resiliency, in which the cornea of the host holds the graft, it is the graft that holds the thin cornea of the host around it. In these circumstances, the displacement of the whole graft, or part of the edge of the graft, is not infrequent. In order to prevent this displacement of the graft, two essential points must be observed in placing the sutures: 1. The sutures must be placed near the edge of the incision. 2. The distance between the sutures must be shorter than the diameter of the graft.

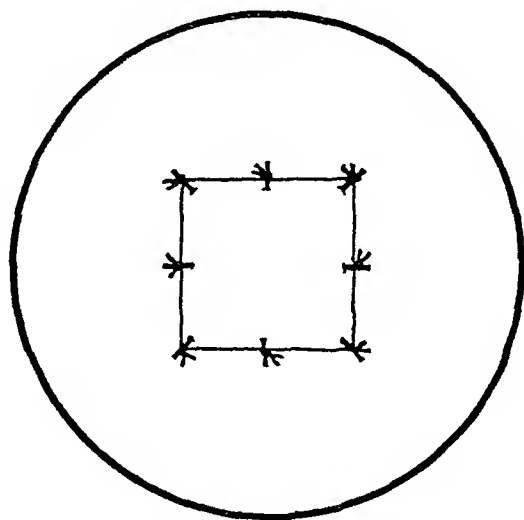


Fig. 9.—Diagram showing border to border suturing in a square transplant.

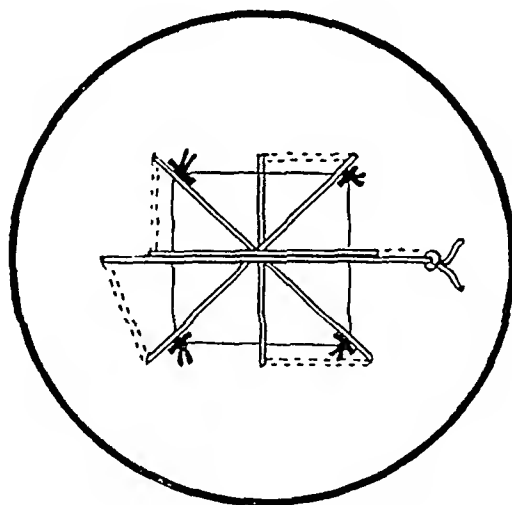


Fig. 10.—Diagram showing Castroviejo's continuous suture to hold the graft in position, reinforced by four border to border sutures placed in the corners of the graft to prevent its displacement.

In spite of these precautions to prevent displacement of the graft, it is sometimes difficult to hold the graft in position in cases of large grafts. In such cases direct suturing of the border of the cornea of the host to that of the donor is recommended. At least four sutures placed in the corners of the square graft, or at the ends of two perpendicular diameters in the circular grafts, are advisable (fig. 10).

Another essential point which must be observed in operation for keratoconus concerns the type of donor material to be used. Since in case of keratoconus with thin cornea it is not the cornea of the host which holds the graft in place, but the graft that holds the cornea of the host around it, it is preferable that the graft be obtained from adult eyes. Younger material from fetuses, stillborn infants or infants does not have enough resiliency to hold the cornea of the host around the borders of the graft.

In cases of eccentric keratoconus extending toward the limbus, the graft must be displaced off center to coincide with the position of the deformity. In these cases the graft must be large enough to permit enclosing the pupillary area within the graft; otherwise, the scarring at the edges of the graft will interfere with vision. Of the circular and square grafts, the square graft placed with the corners as illustrated in figure 4 *A* is preferable, because it includes not only the displaced conus, but also the central area of cornea, most desirable for useful vision.

#### POSTOPERATIVE RECOVERY

During the postoperative recovery, there is more danger of displacement of the graft in eyes operated on for keratoconus than in eyes operated on for other corneal conditions with normal corneal thickness, in which smaller grafts are used. For this reason, the patient should have both eyes bandaged and remain quiet in bed, with fluid and semi-fluid diet, for about seven days. During this period the eye should not be examined. Examination of the eye prior to the seventh postoperative day increases the danger of complications, particularly displacement of the graft, with development of anterior synechias. On the seventh postoperative day, the eye is examined for the first time and penicillin ointment and ointment containing 1 per cent atropine sulfate are applied to dilate the pupil. The reactions of the patient are tested at this time. If the patient is quiet, and not tense, and gives good cooperation, permitting examination of the eye without blepharospasm, the sutures can be removed the following day, with use of local anesthesia. But if the patient is tense, of the high-strung type, with pronounced blepharospasm—a “squeezer”—the sutures should be removed the following day with the use of general anesthesia, preferably that produced by thio-pental sodium. The purpose of applying atropine is to obtain dilation of the pupil, for, in the case of keratoconus with thin cornea, at the time the corneal sutures are removed there may be a collapse of the anterior chamber with loss of aqueous humor, due to slight dehiscence of the incision. Seldom, however, is this opening extensive, and the transplant almost always cicatrizes well in spite of the collapse of the anterior chamber and without complications such as development of

anterior synechia. An anterior synechia is less likely to occur if the pupil has been widely dilated prior to the removal of sutures with the use of atropine sulfate.

The development of an anterior synechia is one of the most frequent complications in keratoplasty for the treatment of keratoconus. If the synechia is smaller than 2 mm., occasionally the use of atropine or physostigmine loosens it. If the synechia is more extensive, surgical intervention will be necessitated in order to prevent opacification, vascularization of the graft and, often, secondary glaucoma. The surgical treatment of the synechia must not be carried out before the fourteenth postoperative day because until then the union of the graft with the cornea of the host is not firm and premature surgical procedures might lead to dislocation of the graft. The operation, however, should not be delayed beyond three weeks, otherwise the graft may already have become opaque on account of the synechia. Therefore, the best time to carry out this procedure is in the third postoperative week, preferably with the patient under general anesthesia.

#### SURGICAL TECHNIQUES FOR TREATMENT OF ANTERIOR SYNECHIAS

If the synechia extends from one fifth to one half of the circumference of the graft, the operation of choice is as follows:

Depending on the location of the synechia, the incision in the sclera is made in the quadrant nearest the synechia: in the lower temporal for synechia in the lower half of the transplant; in the upper temporal for synechia in the upper half. A routine preparation of the eye, about one hour before the operation, is made with instillation of 3 per cent atropine sulfate and 10 per cent phenylephrine hydrochloride, in order to obtain as wide a dilation of the pupil as possible. At the time of the operation, after routine preparation of the eye, 25 per cent mild silver protein U. S. P., a 4 per cent solution of cocaine and a solution of epinephrine hydrochloride (1:1,000) are instilled into the eye. A few drops of the cocaine solution and the epinephrine hydrochloride are injected under the bulbar conjunctiva (fig. 11 *A*) for the purpose of obtaining ischemia and wider dilation of the pupil and of counteracting a tendency to contraction after the anterior chamber has been opened.

An incision is made through the conjunctiva and Tenon's capsule, about 7 mm. from the limbus and parallel to it (fig. 11 *B*). Two 00 silk sutures are inserted in the sclera 4 and 6 mm., respectively, from the limbus and parallel to it. These sutures are used for fixation; one of them is held by the assistant and the other by the surgeon. The area of the sclera between the two sutures is treated by superficial electrocoagulation or by a hot probe to obtain a bloodless operative field (fig. 11 *B*). With the knife, an incision is made in the sclera similar to that performed for cyclodialysis (fig. 11 *C*). When the



sclera has been perforated and the choroid is reached, a long spatula similar to that used for cyclodialysis, but 15 mm. in length, is introduced through the scleral opening and then between the sclera and the choroid into the anterior chamber. The adherent iris is separated from the cornea with the aid of the spatula (fig. 11 *D*). The spatula is then withdrawn and the tip of a Randolph perforated cannula, with the shape of a cyclodialysis spatula attached to a syringe (fig. 11 *E*), is introduced in the same manner as the spatula into the anterior chamber and air is injected to push the iris away from the cornea. The cannula is then withdrawn and the conjunctival incision closed with a

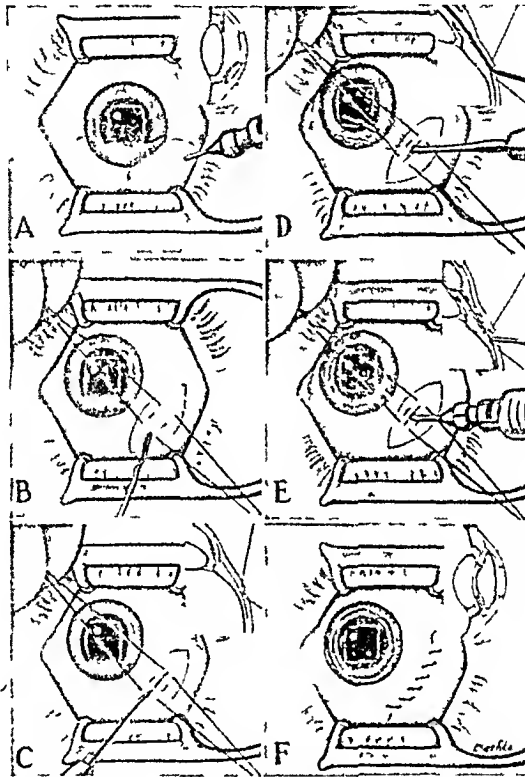


Fig. 11.—Successive steps in the Castroviejo technic for the treatment of moderate anterior synechias.

continuous 000000 silk suture. This cyclodialysis incision placed several millimeters from the limbus is preferable to incisions in the limbus because with the latter it is not always possible to keep the air within the anterior chamber long enough to prevent the recurrence of the synechia.

When the synechia is extensive, the operation which I have found satisfactory is as follows:

The operation should be carried out, preferably, with the patient under general anesthesia. With the aid of scissors and conjunctival forceps, a conjunctival and episcleral flap of 2 to 3 mm. between 10

and 2 o'clock is made around the limbus (fig. 12 *A*). The conjunctival flap is reflected down over the cornea and three 000000 silk sutures mounted in atraumatic needles are inserted, one at 12 o'clock and the other two equidistant from the central one and the ends of the conjunctival incision. The sutures are passed first through the conjunctiva and then through the sclera, entering the sclera about 2 mm. from the limbus and taking a bite of about 1 mm. (fig. 12 *A*). The sutures are now drawn out of the way in order to make the incision with a minimum of interference. With the knife, an ab externo incision is made at the limbus around 12 o'clock (fig. 12 *A*). When the anterior cham-

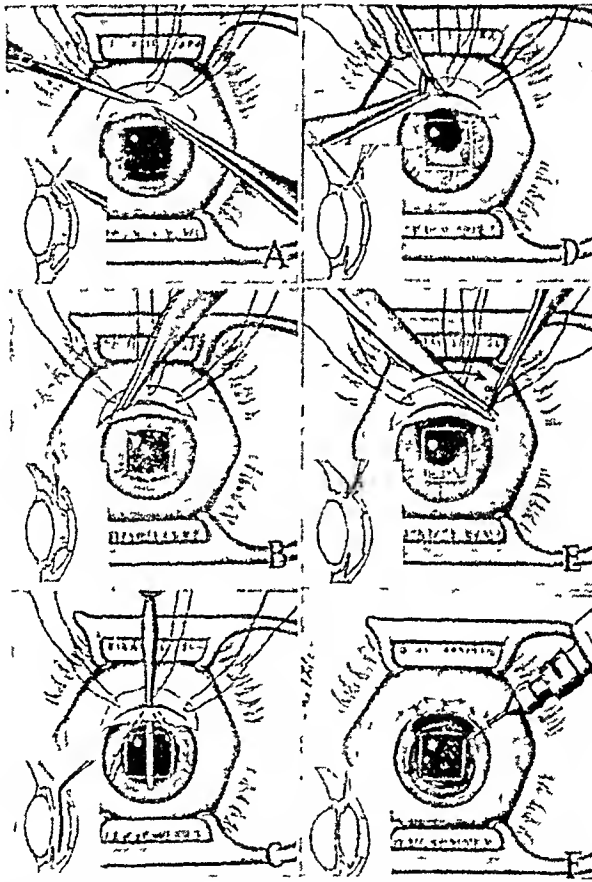


Fig. 12.—Successive steps in the Castroviejo technic for the treatment of extensive anterior synechias.

ber is entered, the incision is enlarged temporally and nasally with the aid of scissors (fig. 12 *B*). With the cyclodialysis spatula, the iris is then separated from the cornea (fig. 12 *C*).

A large iridectomy from 10 to 2 o'clock is then performed (fig. 12 *D* and *E*). The sutures are passed through the corneconjunctival junction, including a small bite of corneal tissue, and tied. Additional conjunctival sutures are inserted, and air is injected into the anterior chamber (fig. 12 *F*) in an effort to push the iris away from the cornea, thus preventing the recurrence of the synechia.

After this procedure, if an anterior synechia develops in the lower half of the graft, the first operation described can be carried out. In several cases in which the two operations were carried out successively, the eye remained without synechias, with a clear transplant and good vision (fig. 13).

In these two operations, bacteria leading to endophthalmitis or panophthalmitis are often introduced into the eye. I have had several such instances; therefore the need of a meticulously aseptic technic and great care in performing these operations should be stressed. Prophylactic treatment with systemic application of penicillin should be carried out, beginning the day prior to the operation and continuing until all the signs of inflammation in the eye have disappeared. In addition, intravenous injections of typhoid vaccine should be instituted.

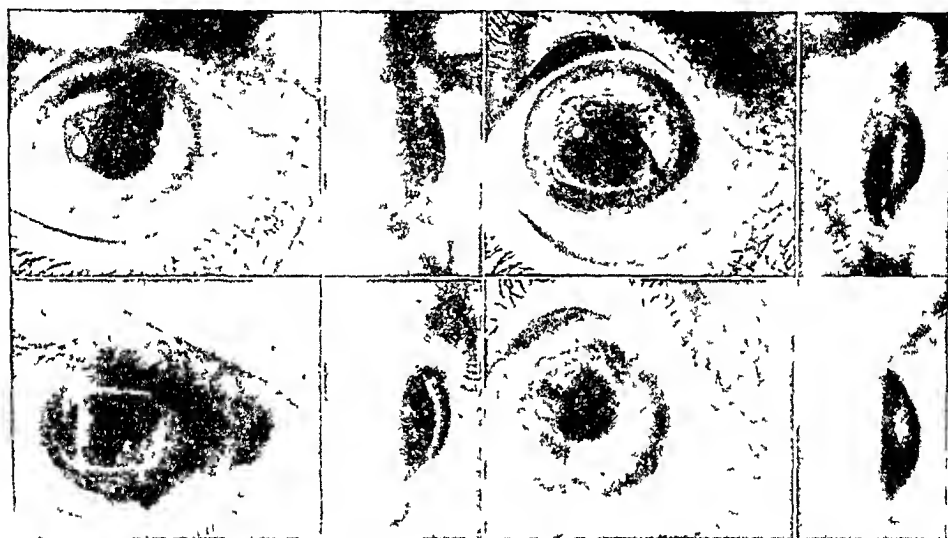


Fig. 13.—Clear transplants after operations for extensive synechia.

In keratoconus, the transplant often has a tendency to protrude during the postoperative course. This must be considered not as a complication, but almost as the normal cicatrization of the grafts in repair of keratoconus.

In order to obtain a more normal curvature, it is necessary to maintain a pressure dressing, which is started on the fifteenth postoperative day and is continued until the fifth or sixth postoperative week. During the first week of the pressure dressing the pressure must not be too strong; otherwise the incision may reopen, leading to development of anterior synechias. However, in the following weeks the pressure can be substantially increased, until as much pressure as possible is applied by the fourth week. It is not necessary, in order to insure adequate pressure, to use bandages of the roll type around the head, which some-

times make the patient very uncomfortable. I have found that the dressing illustrated in figure 14 gives adequate pressure for about two days. For this pressure dressing to be effective, it should be carried out in the following fashion:

The ocular area within the rim of the orbit should be well packed with gauze and two rows of strips of adhesive tape applied, pressure being exerted with the first strip of adhesive tape, with the second row

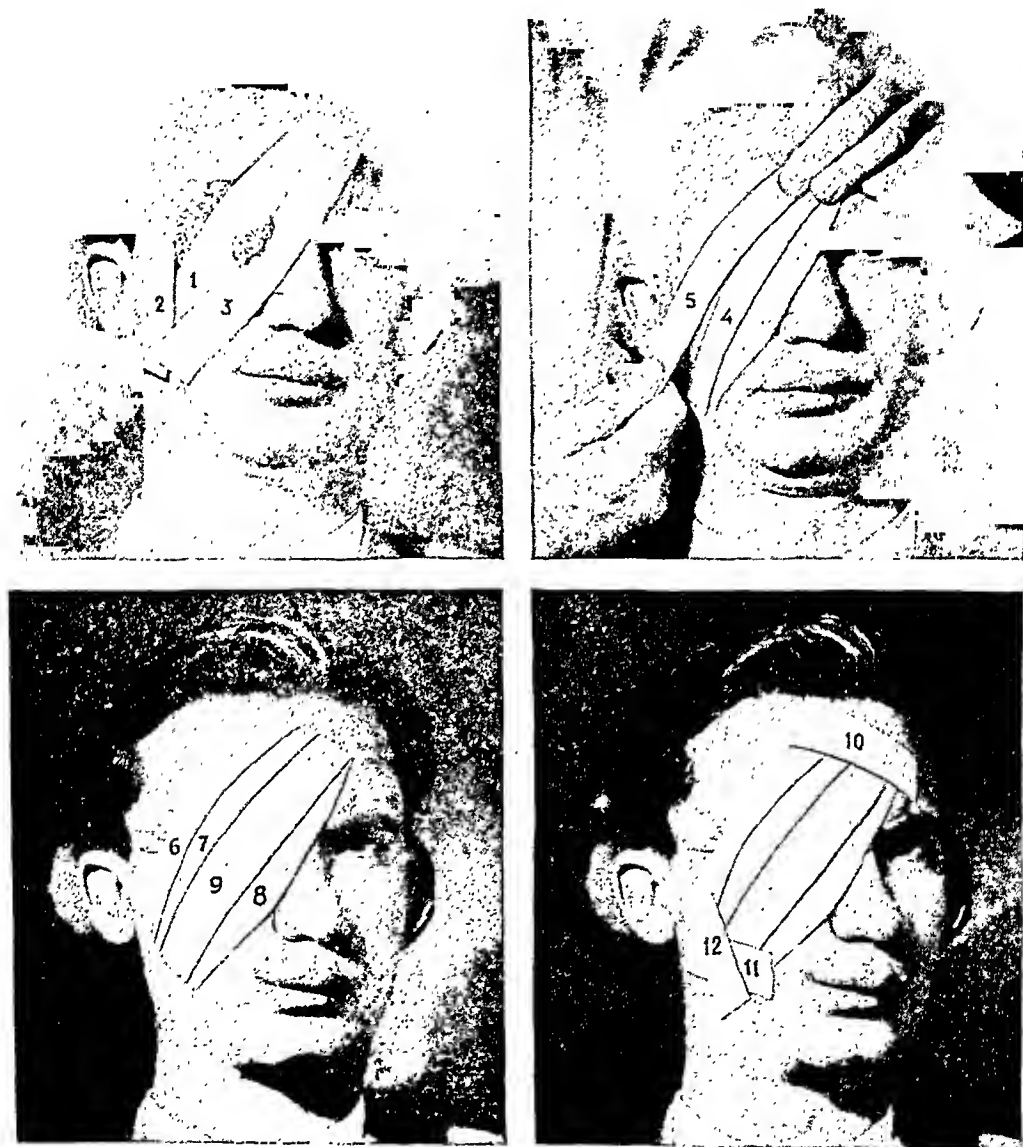


Fig. 14.—Photographs showing successive steps in the application of pressure dressing.

reenforcing the pressure obtained with the first row. The ends of the adhesive tape on the cheek and on the forehead should be held tightly in position by other strips of adhesive tape in order to prevent curling of the edges and loosening of the bandage.

With this pressure dressing, a good curvature of the cornea may already have been obtained by the fourth postoperative week. The

pressure dressing must then be applied with care, so as not to produce too much pressure and to avoid excessive flattening of the cornea, which might result in high hypermetropia, astigmatism or even contact of the cornea with the iris and the development of anterior synechias.

The same type of pressure bandage has been found useful in the treatment of acute ectasia or hydrops, a frequent complication of keratoconus. The bandage is continued until the ectasia has entirely disappeared and the eye has become quiet (fig. 15).

Sometimes in keratoconus, with more frequency than in any other corneal deformity treated by corneal transplantation, the transplant remains protruding for over four weeks in spite of the pressure dressing, apparently owing to the thinness of the edge in the recipient cornea. In these circumstances, the nutrition of the graft is impaired, often

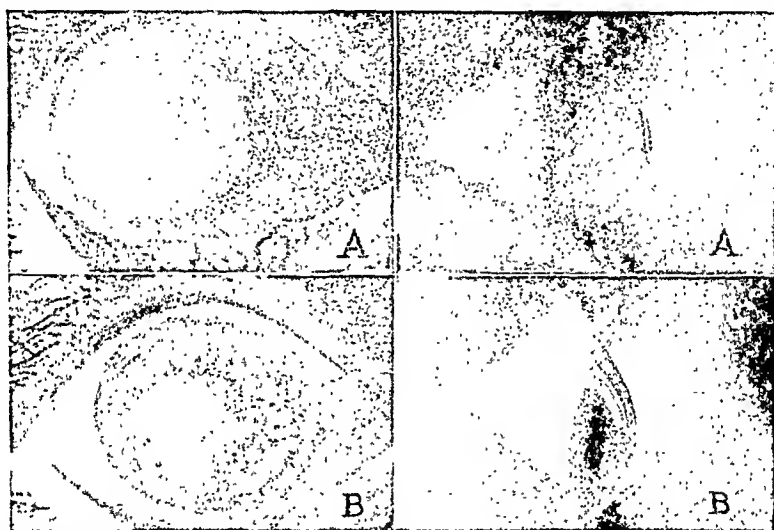


Fig. 15.—Photographs of acute ectasia before (A) and after (B) application of pressure dressing.

leading to cloudiness of the graft and occasionally to the development of corneal edema with bullous degeneration of the epithelium. This corneal edema is generally improved by applications of hypertonic sodium chloride, as a 15 per cent jelly, from three to six times daily. If the bullous degeneration of the epithelium fails to clear up with this conservative treatment, it is advisable to scrape the epithelium and treat the denuded area and about 1 or 2 mm. of the surrounding cornea with light superficial electrodesiccation. With this treatment, the bullous degeneration of the epithelium will disappear, but at the expense of permanent superficial cloudiness of the graft, which will require further surgical correction if the cloudiness is sufficient to impair vision greatly.

If, in spite of the application of pressure dressing, the transplant should cicatrize with protrusion, or uneven curvature, resulting in pro-

nounced myopia and astigmatism, although preserving permanent transparency, the operation is a failure for visual purposes. Contact lenses may occasionally help this situation; if not, a second transplant, preferably larger than the first, will be necessary.

I have mentioned here only the complications most likely to occur in operations for keratoconus. Other complications observed in corneal transplantation have been discussed in another article.<sup>39</sup>

#### RETRANSPLANTATION

If the transplant should become cloudy, because of protrusion during postoperative recovery, anterior synechias successfully treated surgically or postoperative uveitis, but no complication, such as opacity or vascularization, has developed in the surrounding cornea, the eye is still

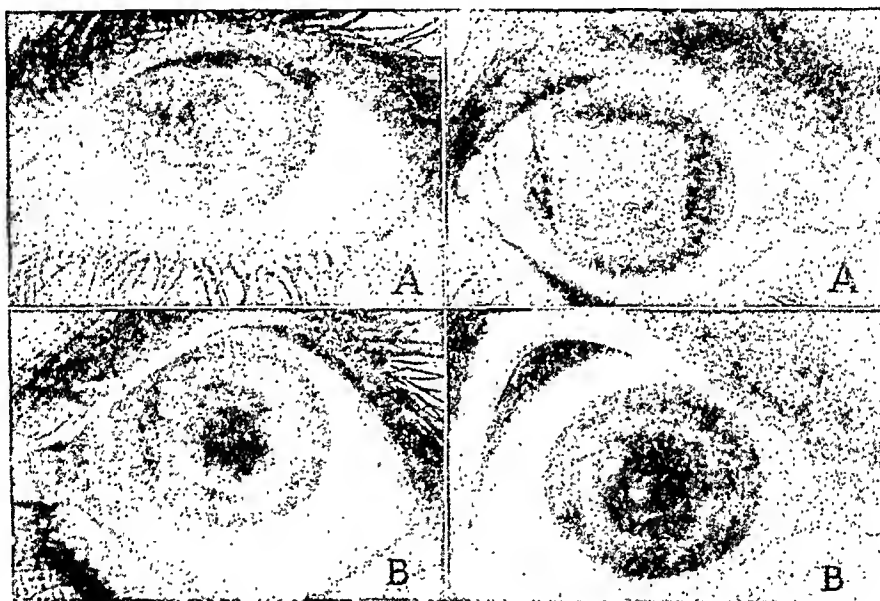


Fig. 16.—*A*, cloudy transplants, and *B*, clear retransplants.

favorable for another corneal transplant. At least six months, but preferably a year, should elapse, however, before the second transplantation, in order to provide time for the eye to become entirely quiet. Figure 16 shows transplants which remained clear after a second operation, when the previous one had resulted in a cloudy graft.

#### CLOUDINESS OF THE GRAFT

In cases of delayed cicatrization due to protrusion or complicating uveitis, the transplant may become cloudy to the point where the patient can see only to count fingers or distinguish hand movements at 1 foot, but sometimes these transplants clear up in a few months to such an extent that it is no longer possible to detect any cloudiness of the graft,

39. Castroviejo, R.: *Tr. Am. Acad. Ophth. & Otol.* 1948, pp. 322-330.

with vision improving sometimes to 20/30, and even 20/20 (fig. 17). This clearing-up process can be expected to take place within a year after the operation. Any opacity remaining after the first year may be considered permanent, requiring further surgical treatment if vision remains poor.

In some cases of extremely pronounced keratoconus, approaching keratoglobus in appearance, I have tried to flatten the cornea by superficial electrodesiccation in order to obtain more normal curvature and render the eye more favorable for keratoplasty. So far, however, this procedure has always resulted in failure.

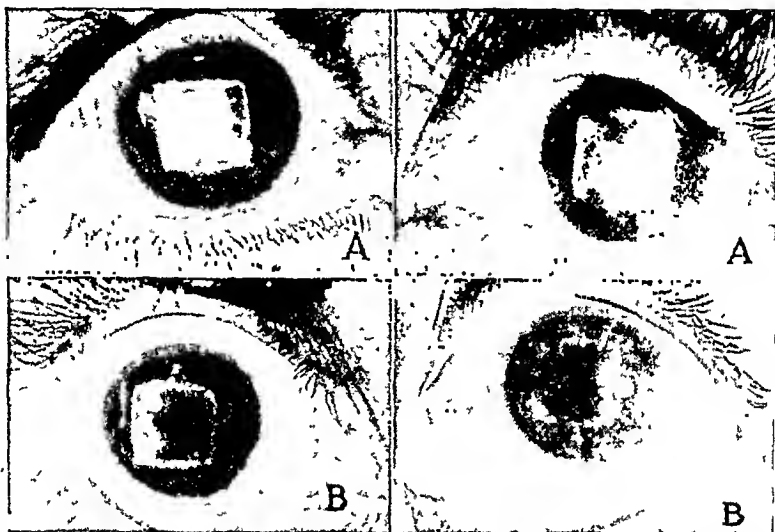


Fig. 17.—Cloudy transplants (*A*), after uveitis, which finally cleared up (*B*).

#### COMMENT

I am convinced that partial penetrating keratoplasty is the treatment of choice for advanced keratoconus. When a suitable technic is used, the percentage of cases of permanently greatly improved vision should be high, from 75 to 90 per cent. The percentage of successful cases will, of course, be higher the more experienced and skilled the surgeon. The surgeon less experienced in keratoplasty given the proper selection of cases and technic, and taking into consideration the observations here presented, may also expect a high percentage of satisfactory results.

9 East Ninety-First Street.

# UNILATERAL THROMBOSIS OF A CAVERNOUS SINUS TREATED WITH PENICILLIN AND SULFADIAZINE

Report of a Case with Follow-Up Study

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AND

JEROME A. GANS, M.D.

CLEVELAND

**I**N THE prechemotherapeutic era thrombosis of a cavernous sinus was a condition with an extremely grave prognosis. Whether septic or aseptic, thrombosis of a cavernous sinus carried with it a high mortality. Therapy was mainly expectant and palliative. The clinical course of the disease has been well described by Lyle<sup>1</sup>:

Early symptoms on the part of the eye are caused by interference with the venous drainage from the eye and orbit. There is discoloration and swelling of the lids with exophthalmos. The conjunctiva is congested. The orbit shows increasing edema with gradual immobilization of the eyes, both from orbital swelling and involvement of the third, fourth and sixth nerves in the sinus. Ophthalmoscopic examination shows an initial edema of the retina with dilated veins. Papilledema is not uncommon. Retinal hemorrhages are occasionally present. As the condition progresses, the media becomes hazy so that the fundus cannot be seen. Pain in the orbit is usually marked. Later, the patient passes into a comatose state with fever and other symptoms of systemic involvement.

Dandy<sup>2</sup> stated that extension to the opposite cavernous sinus through the circular sinus and backward to the lateral sinus occurred in about half the cases. Venous ligation in the neck was frequently necessary to prevent dissemination of metastatic septic emboli. Meningitis and death were so common as to be considered the rule.<sup>3</sup>

Chemotherapy has produced a notable change in this morbid picture. The following case history of unilateral thrombosis of a cavernous sinus following skull fracture is illustrative.

## REPORT OF CASE

Mr. J. N., a white man aged 58, presented himself at our offices with a history of left-sided frontal headache radiating to the occiput, which had begun overnight

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1. Lyle, D. J.: *Neuro-Ophthalmology*, Springfield, Ill., Charles C Thomas, Publisher, 1945.

2. Dandy, W. E., in Lewis, D.: *Practice of Surgery*, Hagerstown, Md., W. F. Prior Company, Inc., vol. 12, chap. 1, p. 425.

3. Eagleton, W. P.: *Cavernous Sinus Thrombophlebitis*, New York, The Macmillan Company, 1926.



about two weeks previously. The headache was almost constant, was not accompanied with nausea or vomiting and was not relieved by simple home remedies, such as acetylsalicylic acid. After the first week of the headache, tinnitus had appeared in the left ear, and in the two days prior to his first office visit the patient had noted diplopia and some redness of his left eye, which prompted him to seek medical attention. There was no history of infection about the face, and at this time the patient could not recall having received any trauma. The past history was essentially without significance except for asthma five years previously, which was relieved by desensitization therapy.

Ocular examination revealed the following condition: Vision was 20/20 in each eye. There was mild conjunctival injection of the left eye with slight chemosis below. There was no proptosis. There was complete paralysis of abduction of the left eye, but other extraocular movements were entirely normal. Both pupils reacted normally to light and in accommodation. Both fundi were entirely normal in appearance. Visual fields taken with a 3 mm. white target at 330 mm. were normal, and the blindspots were of normal size and configuration. In the few days that followed, the chemosis increased, the retinal veins became



Fig. 1.—Appearance of the patient on admission to the hospital. (A) The conjunctival prolapse, edema and ptosis are apparent. (B) The patient was instructed to look to the left. The paralysis of the left abducens nerve is apparent.

slightly fuller on the left and ptosis and proptosis began to appear, so that on May 1, 1947 the patient was admitted to Mount Sinai Hospital for study and treatment.

On his admission to the hospital, physical examination revealed a well developed, well nourished white man, whose alertness was somewhat dulled and who complained of headache in the left frontal area but was in no distress. The left orbit was edematous; the lower bulbar conjunctiva was chemotic and prolapsed, and his left eye was proptosed, as shown in figure 1 A and B. There was no fluctuation in the left orbit and no bruit was audible. The temperature on admission was 99.2 F; the pulse rate was 82 and the respiratory rate 20. His blood pressure was 138 mm. of mercury systolic and 80 mm. of mercury diastolic. Except for the ocular changes, the physical and neurologic condition was entirely normal. Treatment was started with parenteral administration of 320,000 units of penicillin daily in divided doses. On the second hospital day, a roentgenogram of the skull revealed a linear fracture of 7 cm. in the left half of the occipital bone, as seen in figure 2. There was no fragmentation or depression. The orbits were intact, and there was no evidence of fracture of the walls of the maxillary sinuses or zygomas. Confronted with the roentgenographic findings, the patient vaguely recalled that three weeks prior to admission

he had fallen and struck the left side of his forehead on a curb and that his headache seemed to date from the following morning.

On the fourth hospital day, the orbital edema had increased to such an extent that the left eye was completely immobile and the nerve head was very pale, and not elevated. Scattered hemorrhages were seen in the left fundus. Oral administration of sulfadiazine in an initial dose of 2 Gm., followed by 1 Gm. every four hours, was added to penicillin therapy (so long as sulfadiazine was being given, repeated determinations of the blood level showed between 4.1 and 8.4 mg. of sulfadiazine per hundred cubic centimeters). The outer canthus was divided surgically in an effort to reduce pressure of the lids on the globe. On the fifth hospital day a lumbar puncture was made. The spinal fluid was clear; the pressure

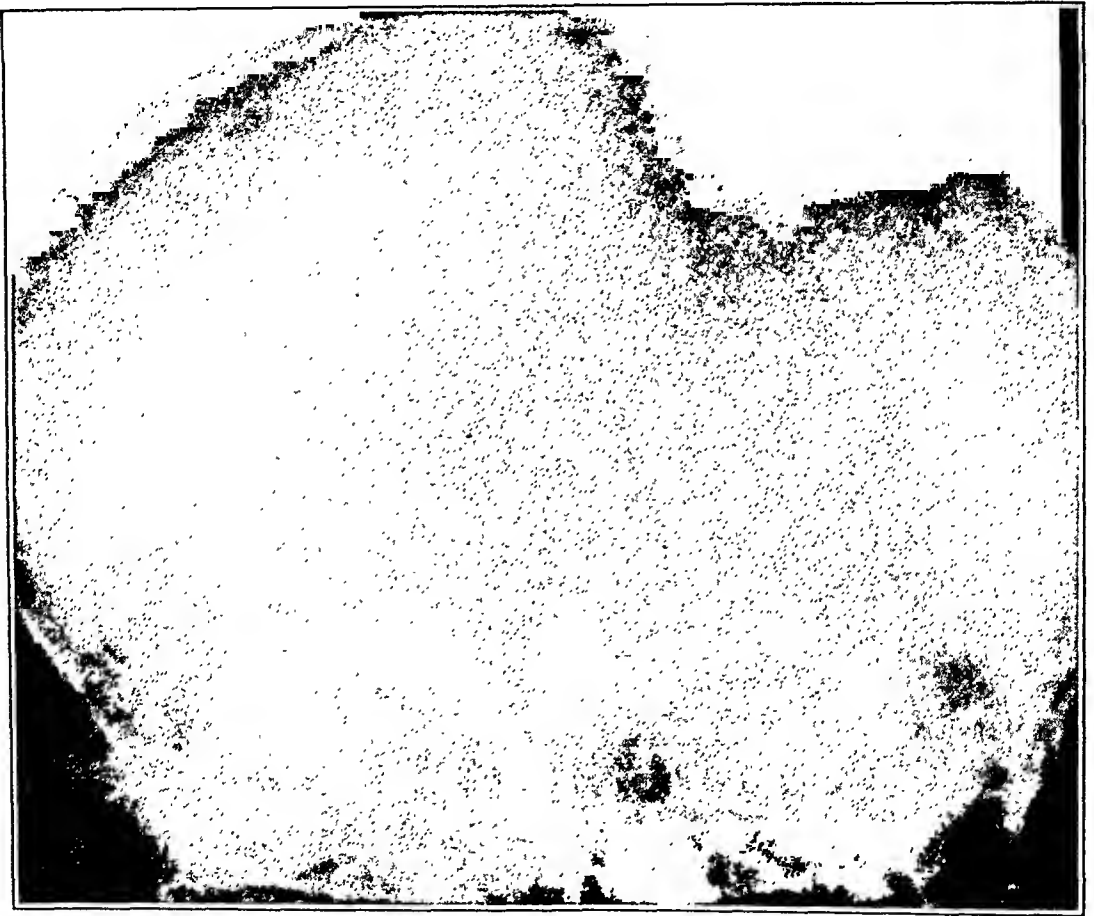


Fig. 2.—Roentgenogram of the skull revealing a linear fracture of 7 cm. in the occipital bone, without fragmentation or depression. The orbits were intact, as were the walls of the maxillary sinuses and the zygomas.

was 160 mm. of water; there were 3 cells per cubic millimeter, and the Pandy test gave a 4 plus reaction for globulin. Protein nitrogen measured 9.8 mg. and total proteins 61.3 mg., per hundred cubic centimeters; the colloidal gold curve was 11112211000, and the gum mastic curve was 3322111000. Diagnostic and exclusion Kline tests gave negative reactions. The orbit was probed with a trocar superonasally in the hope of locating and evacuating an abscess, but without success. On the seventh hospital day, the orbital edema showed no improvement, the cornea was clear but vision had become greatly diminished. The vitreous had become too cloudy to permit visualization of the fundus. On the eighth hospital day, there was no light perception in the left eye.

For the next month the patient was maintained on intermittent therapy with combined penicillin and sulfadiazine. In all, 8,470,000 units of penicillin and 179 Gm. of sulfadiazine were given. Each time that chemotherapy was discontinued the temperature became somewhat elevated; when chemotherapy was reinstituted, the patient again became afebrile. The orbital edema was slow to recede. On several occasions the orbit was incised in different quadrants and probed in search of pus, but none was found. Although the media cleared sufficiently to permit visualization of the fundus, light perception did not return. The disk became a pale lemon yellow with hazy borders and glial proliferation along the large veins. On the thirty-ninth hospital day, the patient was discharged from the hospital with instructions to continue taking 1 Gm. of sulfadiazine by mouth four times a day. All therapy was discontinued after twelve days (approximately two months after the injury), at which time the eye was still completely immobile and the disk pale, with scattered hemorrhages throughout the fundus, and an indurated tongue of conjunctiva still prolapsed through the palpebral fissure.

Three months after the onset, there was some return of mobility of the extraocular muscles of the left eye (30 degrees in vertical range and 20 degrees

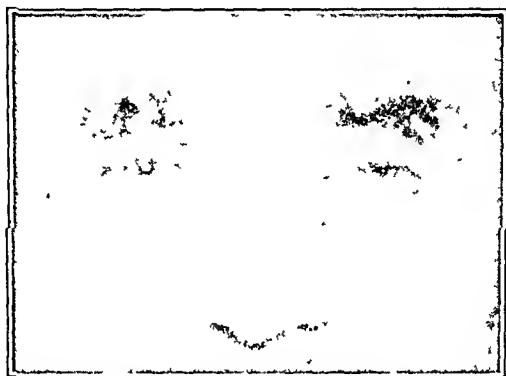


Fig. 3.—Residual ptosis a year after the onset. See text for description of fundus.

in horizontal range); muscular recovery appeared to be general, rather than localized to specific muscles, muscle groups or nerves. Four months after the onset the mobility had increased somewhat more, the pupil was still fixed at a diameter of 3.5 mm. and did not react to any stimulus, either directly or consensually. The disk was yellow white with glial proliferation along the great veins. There were scattered deep hemorrhages with a few strands of proliferating retinitis. The arteries were almost completely invisible; there was only a faint thread of blood in the veins. Beyond the first branching of the superior temporal vein, the vein was completely covered with creamy yellow exudate. There was still no perception of light, and some conjunctival edema persisted. Residual ptosis of the left lid remained.

One year after the onset there was still mild ptosis, as seen in figure 3. The pupil was 3 mm. in diameter and did not react to light directly or consensually. From the central position the left eye moved 30 degrees laterally, 20 degrees nasally, 30 degrees upward and 35 degrees downward. The disk was pale grayish yellow and sharp in outline. The arteries were practically empty and carried only a faint thread of blood. The veins were empty, sheathed and almost free of blood, many appearing only as ghosts of vessels. There were

mobilization of pigment and stippling in the macula, and lesser stippling in peripheral areas of the fundus. There was increased prominence of the choroidal pattern secondary to retinal atrophy, as well as moderate choroidal sclerosis temporal to the macula.

#### COMMENT

This case differed from the usual septic thrombosis in several ways. The onset was insidious, the full picture requiring over three weeks to develop. The course was only mildly febrile, as compared with the usual septic type. The cause was obscure until roentgenograms revealed the presence of skull fracture. Headache, unilateral paralysis of the sixth nerve and faint homolateral conjunctival edema were the only early signs and symptoms. The ophthalmoscopic picture and visual fields were of little value in diagnosis until other signs had already indicated the true nature of the disease. This lack of significance of ophthalmoscopic findings coincided with the experience of Walsh,<sup>4</sup> who stated that "the ophthalmoscopic visible changes are of little importance in establishing the diagnosis. The signs which are observed are engorgement of the retinal veins and low grade papilledema, but these changes appear later."

The fact that this patient survived rather than succumbed to his disease is of more than passing note. With the advent of chemotherapy, the increasing reports of such survivals lend encouragement in the therapy of this grave condition. Reid and McGuckin<sup>5</sup> reported 6 consecutive cases of recovery from thrombosis of the cavernous sinus treated with penicillin and sulfonamide compounds. While the number of reported recoveries is now increasing, the follow-up shows that the condition leaves serious residua. In the case here reported there was complete blindness on the affected side, with internal ophthalmoplegia, partial external ophthalmoplegia and ptosis, still present a year after the illness. Welty<sup>6</sup> reported the case of a 13 year old boy with unilateral septic thrombosis of the cavernous sinus resulting from a furuncle of the ala nasi. Treatment with 36 Gm. of sulfadiazine, 280,000 units of heparin and 3,600,000 units of penicillin brought about a clinical recovery, but the resultant vision was 6/12 and there were residual ptosis and paralysis of the external rectus muscle. Greenish<sup>7</sup> reported

4. Walsh, F. B.: *Clinical Neuro-Ophthalmology*, Baltimore, Williams & Wilkins Company, 1947.

5. Reid, J. L., and McGuckin, F.: Cavernous Sinus Thrombophlebitis: A Report of Six Consecutive Recoveries, *J. Laryng. & Otol.* **61**:273, 1946.

6. Welty, R. F.: Bacterial Thrombophlebitis of a Cavernous Sinus with Recovery, *Arch. Otolaryng.* **43**:70 (Jan.) 1946.

7. Greenish, B. V. I.: Cavernous Sinus Thrombosis, *Brit. M. J.* **1**:876, 1945.

a case of thrombosis of the cavernous sinus complicating erysipelas which responded to therapy with 34 Gm. of sulfathiazole and 1,320,000 units of penicillin. There were resultant paralysis of the sixth nerve and double vision. Walsh<sup>4</sup> cited the case of a boy with septic thrombosis of the cavernous sinus with pathogens present on blood culture, who continued to have exophthalmos and paralysis of extraocular muscles six months after discharge. His final visual acuity was 20/100, although the factor of keratitis may have contributed to the lowering of the visual acuity.

Circulatory stasis and infection are the two major factors that determine the outcome of thrombosis of the cavernous sinus. The high mortality rates previously observed from this condition were due primarily to the element of infection, which produced death either by direct extension, through the development of meningitis, or by promotion of further thrombosis and the dissemination of septic emboli. When the responsible organisms are sensitive to chemotherapy (and for the most part they are), the combined use of penicillin and sulfonamide derivatives promotes recovery from the infectious process. Despite the rapid development of a localizing barrier of chemotherapy, however, it may require considerable time for infection deep within the thrombus to be eradicated. Such foci may light up again if chemotherapy is prematurely discontinued, and even with the infection completely sterilized it requires weeks for canalization of the thrombus to take place. Almost the entire venous drainage of the orbit empties into the cavernous sinus; collateral drainage is practically nonexistent. Thus, obstruction of the cavernous sinus produces absolute orbital stasis and edema, which lead to severe damage of the optic and other cranial nerves and of the retinal elements. While other structures of the orbit and the wall of the sinus may survive a prolonged cessation of circulation, the cranial nerves and retina are highly susceptible to injury, and their recovery is generally incomplete. Varying degrees of blindness and ophthalmoplegia are the inevitable results.

Early institution of anticoagulant therapy to maintain circulation in cases of incomplete thrombosis may be of value. Even in complete thrombosis it may stop further longitudinal extension of the thrombus. Heparin and dicumarol<sup>®</sup> (3,3'-methylene-bis-[4-hydroxycoumarin]) have been so used, with good therapeutic response. The contraindication to anticoagulant therapy is the danger of hemorrhage. In cases of thrombosis arising secondary to infection, in which it is presumed that the danger of hemorrhage is not great, anticoagulant therapy may well minimize damage to cranial nerves and preserve vision. In the case

here reported in which the cause was traumatic, and with the presence of a long fracture of the skull, the risk of hemorrhage was considered too great to use anticoagulants.

In the light of this report, and the many others that are appearing on chemotherapy in cavernous sinus thrombosis, we may safely adopt new concepts of the incidence of mortality in this disease. The rare survival previously noted is now the usual and expected outcome. However, the residua are still severe enough to warrant concern. Early institution of combined penicillin and sulfonamide therapy with the addition of anticoagulants (unless contraindicated) may favor more complete recovery.

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## HERPES ZOSTER OPHTHALMICUS SINE ERUPTIONE

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IN AN exhaustive ophthalmologic review of herpes zoster ophthalmicus, published in the ARCHIVES, Edgerton<sup>1</sup> wrote:

Cases of zoster without eruption are exceptional, although Lederer in 1900, reported such cases. . . . A typical zoster without eruption but with neuralgia may occur. . . . Ahlström, in 1904, described an unusual case in which corneal zoster was the only form of involvement of the fifth nerve in the course of zoster of the lumbar plexus. Von Hoffmann, in 1879, described a similar case, but without the cutaneous eruption.<sup>2</sup>

Although I have not had recourse to all the articles cited, I have the definite impression that herpes zoster ophthalmicus sine eruptione is not a common disorder.

In three years of ophthalmologic practice since World War II, I have encountered 5 cases of herpes zoster ophthalmicus—3 with eruption and 2 without. Brief reports of the 2 cases without eruption, with notes of comparison, follow.

### REPORT OF CASES

CASE 1.—A white man aged 66, a watchman, with hypertensive cardiovascular disease, who eventually succumbed to this condition, complained of bitter neuralgic pains over, in and around his right eye. The pain radiated back into the occiput and down into the right malar region and the right side of the nose. The onset was sudden. There were no prodromal symptoms except malaise. His other complaints were tearing and photophobia of the right eye. His past history was noncontributory except for the hypertensive cardiovascular disease.

The patient had bilateral compound hypermetropic astigmatism with presbyopia, and vision was easily corrected to normal for both near and far in each eye. There were obvious tearing, photophobia and blepharospasm of the right eye. This eye was very slightly exophthalmic. On first examination, all other findings were normal, including results of the usual laboratory tests and the usual ophthalmologic survey with studies of the visual fields and determination

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1. Edgerton, A.: Herpes Zoster Ophthalmicus, Arch. Ophth. **34**:40-62 (July); 114-153 (Aug.) 1945.

2. Citations in the bibliography were: Lederer, R.: Herpes zoster ophthalmicus ohne Hautaffection, Centralbl. f. prakt. Augenh. **24**:232, 1900. Ahlström, G.: Några komplikationer vid herpes zoster ophthalmicus, Nord. med (Hygiea) **4**:920, 1904. von Hoffmann: Herpes zoster ophthalmicus, Tag. d. Versamml. deutsch. Natur. u. Aèrzte **52**:337, 1879; Med.-Chir. Centralbl. **15**:484, 1880.

of tension. Although reflexes were normal, anisocoria appeared in a few days, the right pupil being corectatic. Subsequently, the cornea of the right eye lost its luster, and there developed moderate inflammation of the right preauricular lymph nodes, which subsided in a week. Later there were swelling and infiltration of the corneal stroma with folds in Bowman's and Descemet's membranes and other signs of involvement of the anterior segment, an aqueous flare, cells in the anterior chamber and edema of the iris. There were corneal anesthesia and anesthesia in the distribution of the three branches of the ophthalmic division of the fifth cranial nerve. The left eye was uninvolved except that ophthalmoscopic study early revealed bilateral angiosclerosis grade 2 in each eye.

The course was stormy, and the condition was not responsive to therapy of any sort; although the mydriasis persisted in the right eye, later atropinization made it impossible to assess further pupillary changes. A diagnosis of herpes zoster ophthalmicus sine eruptione was made, since at no time did a cutaneous rash appear. The corneal lesion finally involved and broke through the epithelium, the ulceration proving as refractive to therapy as the pain and involvement of the anterior segment. Smears and cultures of corneal material were not helpful. Although no virus was cultured, the cytologic picture supported at first a virus etiology, but later a hemolytic staphylococcus appeared as a secondary invader. After two weeks, there was sudden complete paralysis of the third nerve; the ptosis seemed to help the corneal condition for time; but, with partial recovery after a few months, the corneal leukoma, which was still partially ulcerated and now presented slight superficial vascularization, flared up. A median tarsorrhaphy was therefore done. Meanwhile, the ocular pain had abated, as well as the neuralgia and anesthesia, the latter clearing first. After the second week of closure of the lids, terrific ocular pain recurred but was then localized. Freeing of the lids disclosed a partially healed cornea but a glaucomatous eye that no longer had even light perception. The pupil was still dilated and was sluggishly mobile, and a complicated cataract was present.

From then until enucleation there were periods of pain and ulceration and periods without these symptoms, but the two were not necessarily correlated. Residual ptosis and slight exophthalmos remained. After retrobulbar injections of alcohol there was freedom from pain for only a few weeks, and the recurrence necessitated removal of the eyes. The patient's ocular condition was comfortable from then until his death.

CASE 2.—Since many features of this case parallel those of the first case, only the salient ones will be mentioned.

A white man aged 50, a truckman, whose past medical history was normal, presented early complaints and signs identical with those in case 1; but later the pupil of his right (involved) eye became miotic and all attempts to dilate it were futile. The corneal picture and the changes in the anterior segment were similar. The picture in the fundus, however, was of no importance. There was suggested enophthalmos of the right eye, and he likewise had a compound hypermetropic astigmatism with presbyopia in each eye. Correction, which was done early, allowed normal vision for near and far in each eye. There was a similar early homolateral involvement of the preauricular lymph nodes, which subsided in a week. However, complete paralysis of the third nerve did not develop in this case; instead, only the superior branch was involved with weakening of the levator and superior rectus muscles. Recovery of this paralysis was complete in two weeks. The corneal course, although stormy, finally ended in recovery, with a dense leukoma, as in case 1, and superficial vascularization. There were no



eventual synechias or complicated cataract, but vision was reduced to 20/200 for near and far with the best correction. The anesthesia disappeared before pain, as in case 1, and no therapy seemed effective. Throughout the course of disease the tension in the involved eye was lower than that in the healthy eye, but before discharge it approximated that of its fellow eye. There was no residual ptosis or difference in position of the eyes, and a relatively normal pupil finally resulted.

Some of the interesting observations in these 2 cases are compared in the accompanying table. The corneal lesions prevented extensive studies of the fundus.

*Herpes Zoster Ophthalmicus Sine Eruptione*

	Case 1	Case 2
Prodromal symptoms.....	Malaise	Malaise
Symptoms of syndrome.....	Herpes zoster ophthalmicus but no rash	Herpes zoster ophthalmicus but no rash
Homolateral involvement of preauricular lymph nodes	Present early and subsided in one week despite clinical course	Present early and subsided in one week despite clinical course
Side involved.....	Right	Right
Corneal anesthesia.....	+	+
Anesthesia of all three branches of the ophthalmic division of the fifth cranial nerve	+	+
Exophthalmos .....	+	Possibly enophthalmos
Disciform keratitis with ulceration and, later, superficial vascularization	+	+
Involvement of anterior segment with edematous iris	+	+
Pupil .....	Mydriasis	Miosis throughout
Involvement of third cranial nerve	Paralysis of entire third cranial nerve with delayed recovery (3 mo.)	Paralysis of superior branch with rapid recovery (2 wk.)
Skin .....	No rash	No rash
Tension .....	Normal at first; elevated later	Low at first; approached that of fellow eye later
Course and response to therapy...	No response to therapy; anesthesia disappeared before pain; stormy course	No response to therapy; anesthesia disappeared before pain; stormy course
Final result.....	Slight residual ptosis; recurrently ulcerated leukoma; complicated cataract; no synechias; sluggishly mobile pupil; absolute glaucoma with enucleation	No residual ptosis; leukoma; lens normal; no synechias; relatively normal pupil; vision 20/200 for far and near

COMMENT

These 2 cases of herpes zoster ophthalmicus sine eruptione are presented, since such cases are likely to be commoner than reports indicate. As would be expected, the diagnoses in these cases were made on a clinical basis.

There are two main types of herpes zoster ophthalmicus irrespective of the presence of a rash: the epidemic and the symptomatic. The latter is stated to be the commoner and is said to be due to a vascular, toxic, inflammatory, traumatic or neoplastic disorder. The epidemic, or primary, type is thought by many investigators to be due to a virus, but there is no unanimity of opinion about this. Those who support the

virus theory believe that the virus is causative with or without predisposing factors, such as trauma, debility, intercurrent fevers and infections and physical factors, and that this virus is related to the virus of herpes simplex and varicella. However, the viruses of herpes simplex and herpes zoster differ immunologically and in many other ways, but both viruses are believed to spread along the nerves, and changes from both have been observed in the gasserian ganglion. An eruption with a zoster-like distribution has been produced by inoculation with the virus of herpes simplex, but other differences were apparent; all in all, there is little to support the idea that the two viruses are closely related. The elementary bodies of the herpes zoster virus are demonstrable in properly stained films of vesicular fluid and are agglutinable. The intranuclear inclusion bodies are acidophilic. The virus is grown with difficulty, and it is said to produce a potent and lasting immunity. These observations make one wonder whether the recurrent herpes zoster does not have a multiple causation or whether there are not many strains of a basic virus type, or a difference between laboratory and in vivo findings.

The etiologic factor in the present cases is not definitely known. The condition in case 1 may have been on a vascular basis, since the patient had hypertensive vascular disease and died of cardiac failure. But all that can be stated is only speculative. At any rate, the course was pernicious in both cases, certainly worse in the case in which enucleation was finally necessary, but treatment did not seem of much avail in either. Unfortunately, suitable blood from a patient convalescing from herpes zoster was not available, nor was convalescent serum used. Although I have found diphtheria antitoxin of some value in cases of vesicular eruptions of the lid, possibly owing to the herpes simplex virus, here it, too, was ineffective.

The clinical picture in each case was that of anesthesia of the fifth cranial nerve, ophthalmic branch, and disciform keratitis with later edema and loss of epithelium, and resultant superficial vascularization, but never deep vascularization. No vesicles were observed at any time, but the iris showed edema in each case with mydriasis in one case and miosis in the other. No synechias were present in either case. Only the third cranial nerve was involved in each case, and only a branch in case 2. The slight exophthalmos with pupillary enlargement in case 1 leads one to wonder whether stimulation of the sympathetic fibers with depression of the parasympathetic nerve fibers was not a factor. The physiology of these mechanisms is more complicated than some authors would have one believe, for the anatomic ramifications of pupillonerve fibers are manifold. A blind eye with a mobile but enlarged pupil adds to the unusualness of the case. The eye in case 2 seemed slightly enophthalmic, and this with ptosis and miosis again

might be interpreted as depression of the sympathetic nerve supply. One might further speculate as to the neurologic basis of the high tension in the one case and of the subnormal to normal tension in the other. In Edgerton's article such factors are discussed with clarity.

The rarity of cases of this condition, or at least of the reports of such cases, warrants the recording of any case, even though nothing of any therapeutic value is to be gained.

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NOTE.—The following pathologic report, by Dr. H. C. Wilder, on the eye enucleated in case 1 is appended, since it was not available at the time of the original writing. It is interesting in that it supports the vascular theory as a possible cause of the original disturbance, as well as its subsequent accompanying glaucoma.

*Microscopic Study.*—The conjunctiva was hemorrhagic, and its vessels were congested. The corneal epithelium was irregular over a vascular scar, which involved the outer central lamellas. In this region Bowman's membrane was absent. Peripherally there were desquamation of corneal epithelium and a thin pannus. Clumps of mononuclear cells clung to the posterior surface of the cornea, and there was moderate loss of endothelial nuclei. There were precipitated proteins in the anterior chamber. The corneoscleral trabeculae were sclerotic, and Schlemm's canal was at least partially obliterated. Pigment was present in the narrowed intertrabecular spaces. The anterior surface of the atrophic iris was vascularized. Slight vascularization was to be seen in the filtration angle, but there was no actual anterior synechia. The ciliary body was somewhat atrophic. The vascular layer was edematous and contained hemorrhage. The processes were hyalinized and their vessels congested. The choroid was thin and contained a few small patches of lymphocytes. The choroidal arteries were sclerosed and the choroidal veins congested. There were multiple retinal hemorrhages and sclerosis of retinal arteries. The retinal ganglion cells had disappeared. The nerve fiber layer was atrophic, and the outer nuclear and outer plexiform layers were thin. There is advanced retinal atrophy in the macular region. Here the rods and cones had disappeared, and there was considerable loss of normal architecture. The cupped optic disk contained sclerotic arteries. The lamina cribrosa was depressed, and behind it the optic nerve had undergone cavernous atrophy on the temporal side. There was lymphocytic infiltration around episcleral and adherent orbital veins. Although most of the lens had been lost in the technical procedure, there appeared to be early degenerative changes in the subcapsular fibers at the equator and posteriorly.

*Diagnosis.*—The diagnosis was central corneal scar; episcleritis; mild chronic uveitis; arteriosclerosis, and hemorrhagic glaucoma, compatible with occlusion of the central retinal vein or large tributaries in or around the nerve head.

## CORNEAL TRANSPLANTATION

### I. Visual and Cosmetic Results

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“NEW EYES for Old—Corneal Transplants” was the spectacular title of an article published in *Hygeia* last year.<sup>1</sup> According to this article, corneal transplantation is no longer experimental but has been proved in several thousand operations, and the factors making for its success or failure are well established. It also stated that the technic has been improved to the point where it may be undertaken with the same degree of confidence as may any other major operation on the eye. Publicity of this type has misled the public into believing that corneal transplants are a cure for total blindness and that new eyes can be transplanted to replace diseased ones. It is unfortunate that this article appeared in *Hygeia*, a magazine designed for the layman and approved by the medical profession.

The layman is not alone in his lack of knowledge on the subject of corneal transplantation. Many members of the medical profession, including even some ophthalmologists, have been confused by the recent wave of optimistic literature on corneal transplants. One of the principal causes of this optimism has been the tremendous, but unfortunate, publicity surrounding the operation for corneal transplantation during the past decade, particularly in the United States. The force of this publicity has been such that surgeons have been reluctant to publish anything but successful cases. Few failures can be found recorded in the literature. The publication of isolated successful results has been especially misleading, both in professional journals and in the lay press. The point was finally reached where even the more experienced ophthalmologists read so much about successful corneal transplants that they began to believe what they read. The truth is that the important facts about this operation have not been revealed. Among the unanswered questions are these: What are the indications for a corneal transplantation? What is the percentage of successful results? What is the standard of success, transparency of the graft or improvement in vision? What are the complications following this operation? How do these complications affect the final result? The answers to these

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1. Fine, M.: New Eyes for Old: Corneal Transplants, *Hygeia* 25:780-781, 813-814, 1947.

questions cannot be learned in the study of successful cases alone. Complete series of cases, with pertinent data on all cases in which the procedure was attempted, both successes and failures, are needed to evaluate properly a new operation. No such series of corneal transplantations of significant size can be found in the existing literature.

It has been my privilege to review the clinical records of all ward cases of corneal transplantation occurring at the Presbyterian Hospital in the past fifteen years and to see many of the patients after operation in the Vanderbilt Clinic. The thorough preoperative work-up and the long postoperative follow-up of most of these cases make the series very favorable for evaluation. The purpose of the present paper is an analysis of the visual and cosmetic results in this series of cases.

#### REVIEW OF LITERATURE

Although the literature contains many papers on corneal transplantation, few authors have had experience with more than a dozen operations. The notable exceptions are Elschmig, Filatov, Thomas and Castroviejo, each of whom has reported a considerable number of keratoplasties. Perhaps one should also mention Fuchs,<sup>2</sup> who described his experience with 30 corneal transplantations in 1894, and Franceschetti, who has recently reported two series of operations.

Elschnig and Gradle<sup>3</sup> first discussed the results of corneal transplants in 1923, when they reported 9 permanently clear grafts in a series of 93 operations performed in Elschmig's clinic. Later (1930) Elschmig<sup>4</sup> reviewed his entire experience with the operation, covering a period of over twenty years. A total of 174 transplantations were performed in Elschmig's clinic during that period, and all but 7 of these operations were done by Elschmig himself. Thirty-five of the 174 operations were performed for purely cosmetic reasons, and the results in these cases were uniformly poor. Of the remaining 139 transplantations performed for visual purposes, Elschmig reported improved vision in 65 cases (46.7 per cent), opaque grafts in 51 cases (36.7 per cent) and dislocation of the graft in 23 cases (16.6 per cent). He concluded that one should refuse to do the operation in cases of aphakia, on patients under 14 years of age, in eyes with wide anterior synechias and in the presence of glaucoma.

In 1935 Filatov<sup>5</sup> published his results in 96 corneal transplantations performed between 1923 and 1932. He obtained clear grafts in

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2. Fuchs, E.: Ueber Keratoplastik, *Wien. klin. Wchnschr.* 7:843-845, 1894.

3. Elschmig, A., and Gradle, H. S.: History of Keratoplastic Operations to Date, *Am. J. Ophth.* 6:998-999 (Dec.) 1923.

4. Elschmig, A.: Keratoplasty, *Arch. Ophth.* 4:165-173 (Aug.) 1930.

5. Filatov, V. P.: Transplantation of the Cornea, *Arch. Ophth.* 13:321-347 (Feb.) 1935.

14 of this series; in 12 of the 14 cases (12.5 per cent) vision was improved. In 1937 Filatov<sup>6</sup> discussed another series, of 95 operations, performed from 1932 to 1937. He divided his results in this series into four categories, according to the transparency of the grafts: (1) opaque grafts, 46 cases; (2) half-transparent grafts, 27 cases; (3) transparent grafts,<sup>7</sup> 18 cases, and (4) clear grafts with a connective tissue film over the posterior surface, 4 cases. Filatov stated that the percentage of clear grafts in this series was not significant because in 46 cases the condition was hopeless from the beginning (glaucoma, buphthalmos, applanation, atrophy or symblepharon).

In 1937 Thomas<sup>8</sup> summarized his results in 36 corneal transplantations performed between 1930 and 1936. Thomas devised a classification for his results, according to the transparency of the graft, as follows: (1) transparent graft, (2) slight opacity, (3) much opacity, but less than the original, (4) much opacity, but equal to or worse than the original, (5) detached graft and (6) loss of the eye. In his series of 36 operations, there were 5 transparent grafts, 7 grafts with a slight opacity, 9 grafts with much opacity but less than before operation, 14 grafts with much opacity, equal to or less than that before operation, and 1 detached graft. Thomas stated that the results in the first three categories (21 operations, or 58 per cent) were successful.

In 1938 Castroviejo,<sup>9</sup> discussing over 100 corneal transplants performed between 1933 and 1937, reported clear grafts and considerable improvement in visual acuity in over 40 per cent of unselected cases. He found transparent grafts and improved vision in more than 70 per cent of favorable cases. In a summary of more than 150 keratoplasties in 1939, Castroviejo<sup>10</sup> stated that permanently clear grafts and considerable improvement in vision could be expected in more than 90 per cent of suitable cases. Later Castroviejo<sup>11</sup> repeated these impressive

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6. Filatov, V. P.: Transplantation of the Cornea from Preserved Cadaver's Eyes, *Lancet* **1**:1395-1397 (June 12) 1937.

7. Some may question Filatov's definition of a transparent graft. He explained that "transparent graft" meant that the details of the anterior chamber could be clearly made out, at least through part of the transplant, or that there was a good light reflex through the graft.

8. Thomas, J. W. T.: The Results of Corneal Transplantation, *Brit. M. J.* **1**:114-116 (Jan. 16) 1937.

9. Castroviejo, R.: Results of Corneal Transplantation, *Arch. Ophth.* **19**:834-835 (May) 1938.

10. Castroviejo, R.: Present Status of Keratoplasty, *Arch. Ophth.* **22**:114-126 (July) 1939.

11. Castroviejo, R.: (a) Keratoplasty; Comments on Technique of Corneal Transplantation. Source and Preservation of Donor's Material. Report of New Instruments, *Am. J. Ophth.* **24**:1-20 (Jan.), 139-155 (Feb.) 1941. (b) Indications and Contraindications for Keratoplasty and Keratectomies, *Tr. Am. Ophth. Soc.* **43**:324-330, 1945; *Am. J. Ophth.* **29**:1081-1089 (Sept.) 1946.

figures in relation to even larger series of cases. A number of other ophthalmologists<sup>12</sup> in this country have also been enthusiastic about their results with corneal transplantation.

Some of the recent European reports on corneal transplantation have not been so optimistic. In 1943 Franceschetti and Streiff<sup>13</sup> reported their findings in 50 cases of corneal transplantation as follows: improved vision (20/200 or better) in 16 cases; slightly improved vision in 7 cases; no significant change in vision in 17 cases, and a loss of vision in 10 cases. In 1946 Weve<sup>14</sup> pointed out the dangers of the sensational publicity surrounding the operation in the United States and called attention to the great discrepancies between results reported in America and those reported in Europe. He stated that cases favorable for keratoplasty are rare and that the results are generally not very good. Franceschetti and Doret<sup>15</sup> reported their results in another series, of 45 cases, in 1946, as follows: improved vision (20/200 or better) in 14 eyes; slightly improved vision in 11 eyes; no significant change in vision in 17 eyes, and a loss of vision in 3 eyes. In contrast with these reports, Filatov<sup>16</sup> described a great increase in the number of successful operations when he changed from living cornea to cadaver cornea as donor material. According to his text, he performed a total of 842 corneal transplantations between 1922 and 1941. In 171 operations the donor material was taken from living persons, and in 671 operations, from the cadaver. Successful results were obtained in 24.1 per cent of favorable eyes in the first series and in 66.6 per cent of favorable eyes in the second series (cadaver cornea).

The pertinent data on the results of corneal transplantation from the papers cited in this review are assembled in table 1. There are

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12. Fine, M.: Treatment of Keratoconus by Corneal Transplantation, Tr. Pacific Coast Oto-Ophth. Soc. **28**:48-66, 1947. Leahey, B. D.: Corneal Transplantation, New England J. Med. **228**:387-389, 1943. Lordan, J. P.: Ophthalmological Progress: Sight Restoration by Corneal Transplant, California Med. **68**:90-94, 1948. McKinney, J. W.: Indications for Corneal Transplantation, South. Surgeon **13**:622-625, 1947. Paton, R. T.: Sight Restoration Through Corneal Grafting, Sight-Saving Rev. **15**:3-12, 1945; Evaluation of Results in a Series of Corneal Transplants, Arch. Ophth. **33**:83-85 (Jan.) 1945; Technique and Complications of Keratoplasty, Am. J. Ophth. **30**:1302-1303 (Oct.) 1947; Complications Encountered in Keratoplasty, *ibid.* **30**:1436-1439 (Nov.) 1947.

13. Franceschetti, A., and Streiff, E. B.: Résultats fonctionnels dans 50 cas de k ratoplastie avec quelques d tails sur la technique op ratoire, Schweiz. med. Wchnschr. **73**:1371-1374, 1943.

14. Weve, H. J. M.: Clinical Significance of Corneal Transplantation, Nederl. tijdschr. v. geneesk. **90**:1768-1774, 1946.

15. Franceschetti, A., and Doret, M.: Technique et r sultats des greffes de la corn e, Bull. et m m. Soc. fran . d'opht. **59**:83-95, 1940-1946.

16. Filatov, V. P.: Optical Transplantation of the Cornea and Tissue Therapy, Moscow, Markomzdrav, State Publishers of Medical Literature, 1945; reviewed, Arch. Ophth. **37**:698-700 (May) 1947.

many obvious voids. Elschnig and Filatov gave the number of cases in which vision was improved but did not mention their standard of improved vision. Both these surgeons failed to discuss the visual results in the remainder of their series. Thomas discussed transparency of the graft only and paid little attention to visual results. Castroviejo cited no exact figures but gave only approximate numbers of cases and approximate percentages of successful results. He discussed his percentage of successful results in favorable eyes without revealing the number of favorable eyes. Castroviejo quoted the same figure for clear grafts and for eyes with improved vision, lending the

TABLE 1.—*Published Results of Corneal Transplantation*

Author	Number of Cases	Number with Improved Vision	Number of Clear Grafts	Number of Opaque Grafts
Elschnig, 1930.....	139	65, or 46.7%	32, or 23.0% (Partially clear: 33, or 23.7%)	51, or 36.7% (Dislocated graft: 23, or 16.6%)
Filatov, 1935.....	96	12, or 12.5%	14, or 14.6%	.....
Filatov, 1937.....	95	.....	18, or 18.9% (Partially clear: 21, or 22.1%)	46, or 48.4%
Thomas, 1937.....	36	.....	5, or 13.9% (Partially clear: 16, or 44.4%)	14, or 38.9% (Dislocated graft: 1, or 2.8%)
Castroviejo, 1938.....	Over 100	Over 40% in unselected cases Over 70% in favorable cases	.....	.....
Castroviejo, 1939.....	Over 150	Over 90% in favorable eyes	.....	.....
Franceschetti and Streiff, 1943..	50	16, or 32% (Slightly improved: 7, or 14%)	.....	.....
Filatov, 1945.....	171 Living cornea	24.1% in favorable eyes	.....	.....
	671 Cadaver cornea	66.6% in favorable eyes	.....	.....
Franceschetti and Doret, 1946..	45	14, or 31% (Slightly improved: 11, or 24%)	.....	.....

impression that all clear grafts lead to improved vision. Franceschetti and his co-authors alone have reported all the visual results, good and bad, in a complete series of operations. One important factor in the evaluation of this operation, namely, the length of the follow-up period, has been overlooked by all these authors.

#### RECENT SYMPOSIUM

A sober note was finally sounded in this country in 1947, when Post<sup>17</sup> called attention to the need for a critical analysis of corneal transplantation. Soon after, the American Academy of Ophthalmology and Otolaryngology arranged a symposium on this subject, with one

17. Post, L. T.: Eye Banks, Editorial, Am. J. Ophth. 30:920-922 (July) 1947.



paper on the results of the operation. The plan was to collect a large enough number of case reports so that the results would be statistically significant. Representatives of seven ophthalmic clinics assembled the data on corneal transplantations performed in their hospitals and forwarded the information to one institution for transcription to punch cards and statistical analysis. The figures presented by the statistical machines were then interpreted and the report<sup>18</sup> compiled was that delivered at the 1947 meeting of the society.

Although it is generally believed that this statistical study worked well, I do not subscribe to that opinion. Too much emphasis was placed on statistics, and the result was a report with too many statistics and too few facts. In addition to statistical confusion, the report of the symposium failed for the following reasons:

*Postoperative Selection of Cases for Analysis.*—The authority of this cooperative analysis was greatly weakened by the exclusion of a considerable number of cases from evaluation. Moreover, the number of cases so excluded varied in the different analyses. The ensuing variability in the strength of the series is demonstrated by the totals in the five tables in the report; tables 1 to 5 contain, respectively, 362, 367, 357, 331 and 253 cases. A striking example of exclusion of unfavorable cases is seen in the analysis of visual results, in which 128 cases were excluded on the basis of preoperative cataract, glaucoma, nystagmus, amblyopia ex anopsia and pathologic condition of the fundus. One might miss lesions in the fundus in these cases, but how can one disclaim preoperative knowledge of cataract, glaucoma, nystagmus or squint in over one third of the series? Again, when the cases were divided into prognostic groups, 79 cases were placed in group 1 (the very favorable group). However, when the visual results were discussed according to prognosis (on the next page), only 58 cases from this most favorable group qualified for analysis!

*Misleading Use of Percentages.*—All results and conclusions in the report were translated into percentages, regardless of the size of the group being analyzed; most of these percentages had little statistical significance. A percentage has little meaning when the sample from which it is derived is much less than 100. For example, in this report the results of corneal transplantation were judged as good in cases of aphakia, because 42.8 per cent of the grafts in such cases remained clear. Actually, there were only 7 cases of aphakia and 3 clear grafts; a change in 1 graft would have lowered this percentage to 28 per cent or raised it to 57 per cent. Similarly, these dubious percentages were used to compare results in diagnostic groups varying widely in strength

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18. Owens, W. C., and others: *Symposium on Corneal Transplantation: V. Results*, Tr. Am. Acad. Ophth. 52:341-346 (March-April) 1948; Am. J. Ophth. 31:1394-1399 (Nov.) 1948.

(as small as 13 for active keratitis and as large as 141 for nonspecific inflammatory scar), and the percentages were then treated as though of equal statistical significance. Further, all percentages in the report were carried to tenths of a per cent, regardless of the size of the group. These fractions were arithmetical by-products, without meaning, and tended only to increase the apparent significance of already questionable percentages.

*Clear Graft as the Standard of Success.*—The report admitted that the most important consideration in evaluating the result of a corneal transplantation is improvement in vision, but stated that mere comparison of preoperative and postoperative vision is unsatisfactory because some patients have preoperative cataract, glaucoma, nystagmus, amblyopia ex anopsia or lesions of the fundus. Changes in visual acuity as a measure of success were also criticized on the basis that slight changes may be due to increased effort or to familiarity with the test objects. These arguments are difficult to follow. To repeat, an ophthalmologist should generally be aware of the aforementioned conditions before operation, and the results of operation performed in spite of these complications must be faced, just as in a review of cataract extractions. It is true that slight changes in visual acuity are often meaningless. However, the very fact that visual acuity is recorded by means of a numerical scale enables one to eliminate small changes in acuity and makes possible a grading of the significant changes that is quite impossible with transparency of the graft. There are always "slightly cloudy," "hazy" and "almost clear" grafts that defy classification as to transparency. More important, however, is the fact that clear grafts do not necessarily mean a better eye; transparent grafts that bulge enough to prevent useful vision are not uncommon. Except in the unlikely event of transplantation for cosmetic reasons, the only logical index of success for this operation is improvement in vision.

*Paucity of Reported Visual Results.*—No visual results were reported for the whole, unselected series; only the visual outcome in selected fractions of the series received recognition. In one selected group only the number of cases in which visual acuity of 20/20 to 20/30 was obtained and the number of cases in which all light perception was lost were given. In another selected group, the number of cases in which visual acuity was 20/100 or better was given. There was a comparatively detailed discussion of the visual results in the cases with preoperative vision of 20/100 or better; the conclusion that corneal transplantation is not warranted in patients with such acuity was naïve. The section on visual results according to prognosis contained so many statistical and arithmetical inconsistencies that the value of the conclusions drawn is difficult to assess. The most important defect in the

symposium, however, was the omission of an analysis of the visual results in an unselected series.<sup>19</sup>

*Glasses.*—The report contained no reference to optical correction, either preoperative or postoperative. One would like to know whether the visual acuity, before and after operation, was recorded with or without glasses. In the cases with improved vision following the operation, one would like to know the nature of the refraction.

*Brevity of Follow-Up Period.*—The four month period of postoperative observation was short. Six months should elapse before the outcome of a corneal transplantation is at all certain, and successful grafts at the end of six months occasionally become failures after a year or more.

*Summary.*—This cooperative effort to analyze the results of several series of corneal transplantations failed in the same manner that the reports of so many individual series have failed, namely, in the exclusion of unfavorable cases. While admitting that the goal of corneal transplantation is improvement in vision, the authors of this report judged their results on the basis of clarity of the graft. Finally, this statistical analysis contained too many figures of little statistical significance and showed little correlation of its various subdivisions.

### PRESENT SURVEY

In view of the inconclusive nature of the results of the symposium on corneal transplantation, I have again reviewed the records of such operations performed in the ward services at the Institute of Ophthalmology of the Columbia University-Presbyterian Hospital Medical Center. Most of these operations were included in the series discussed in the symposium.<sup>20</sup> The postoperative result has now been observed

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19. Although the visual result in the unselected series was not given in the symposium, it may be estimated with fair accuracy from the data in table 5 of that report.<sup>18</sup> Presuming only that all cases in which vision was improved were included in this table, one may conclude that in the unselected series of 381 cases (1) better than 20/200 visual acuity was obtained in 91 cases, or 24 per cent; (2) slight improvement, but not to better than 20/200, was obtained in 19 cases, or 5 per cent; (3) vision remained better than 20/200 but was unchanged in 3 cases, or 1 per cent; (4) loss of vision to 20/200 or less occurred in 85 cases, or 22 per cent; (5) vision remained 20/200 or less but was unchanged in 55 cases, or 14 per cent, and (6) the visual result was not given but was 20/200 or less in 128 cases, or 34 per cent. More briefly, the postoperative visual acuity was better than 20/200 in 94 cases, or 25 per cent of the series, and was 20/200 or less in 287 cases, or 75 per cent of the series.

20. At that time, the data from the case histories were collected and submitted to the chairman of the committee by Dr. J. A. C. Wadsworth and me. We did not participate, however, in the evaluation of the results or the preparation of the paper read at the meeting of the Academy.

for an additional eighteen months in most cases, and the operations performed during 1947 have been included. In the present review, particular attention is given to the preoperative and the postoperative visual acuity. The best visual acuity, with or without correction, is recorded and the refraction noted. Because the significance of the reported results increases with the length of observation, the follow-up period for each operation is included. The degree of transparency of the graft is included for purposes of comparison.

Before the results in a series of corneal transplantations can be evaluated, the criterion of a successful operation must be determined. Excluding transplantation for cosmetic reasons (a questionable procedure), it must be granted that the goal of the operation is improved function and that clarity of the transplant is but one of the anatomic prerequisites to success, of no more importance than normal curvature of the cornea or absence of anterior synechias. Admitting that improvement in vision is the measure of a good result, it still remains to specify the necessary amount of improvement. In the symposium, changes in visual acuity from light perception to perception of hand movements, from perception of hand movements to the 1/200–10/200 category and from the 1/200–10/200 to the 11/200–20/200 category were tabulated under improved vision. These are very small changes in visual efficiency, however, and the recording of visual acuity in these low categories is subject to considerable error, particularly when both the physician and the patient are trying to show postoperative improvement. Moreover, such changes are not significant so far as industrial vision is concerned. From a practical point of view, then, it appears necessary to decide what constitutes a significant change in vision and to select some point on the scale of visual acuity to serve as a standard of minimum acuity for a successful result. It is suggested that significant changes in visual acuity be arbitrarily limited to changes of more than one step in the visual scale. This can be applied to both increases and decreases in visual acuity. Inasmuch as 20/200 is commonly accepted as the threshold for industrial blindness, it is suggested that a successful result after a corneal transplantation should require improvement in visual acuity to better than 20/200. This will furnish a convenient yardstick for success, acceptable and known to all physicians, from which other graduations of success or failure can easily be computed.

#### STANDARDS FOR EVALUATION OF RESULTS

Employing these two arbitrary provisions, I have devised the following standards for the evaluation of this series of corneal transplantations:

*Improved Vision* (successful result).—Vision is classified as improved when the final visual acuity is (1) better than 20/200 and (2) better than the preoperative visual acuity by more than one step

in the acuity scale. Increases of more than one step in the visual scale when the final result is 20/200 or less are classified as unchanged.<sup>21</sup>

*Unchanged Vision* (not improved, or no significant change).—Vision is said to be unchanged when the final visual acuity fails to differ from the preoperative visual acuity by more than one step in the visual scale, in either direction, and this pertains whether the final visual acuity is better or worse than 20/200. This category also includes those eyes in which there is an increase of more than one step in the visual scale but the final result is 20/200 or less.

*Loss of Vision*.—There is said to be a loss of vision when there is a decrease in visual acuity of more than one step in the visual scale, whether the final result is better or worse than 20/200. This group also includes eyes showing a change from light perception to no light perception.

#### ANALYSIS OF RESULTS

A total of 182 corneal transplantations were performed in the ward services at the Institute of Ophthalmology between 1933 and 1947. Seventeen operations were excluded because the follow-up period was shorter than six months.<sup>22</sup> The remaining 165 operations, performed on 110 patients, form the basis of this report. These operations are divided into eight groups, according to diagnosis, and the pertinent data on results are tabulated by group. The operations on eyes that had already experienced corneal transplantation were placed in a separate group and called secondary transplantations. This appeared appropriate in most instances because the pathologic condition of the cornea at the time of the secondary operation varied so greatly from the original lesion. The numbers in the first column in the tables refer to operations, not to patients or to eyes. In each group, the operations are arranged in chronologic order. The clinic number, age, and sex, serve to identify the patient. The visual acuity given is the best available to that eye, either with or without correction. In a few instances in which visual acuity was recorded with a contact lens, the lens was well tolerated. In a number of cases of keratoconus, vision was improved with contact lenses, but the patient did not tolerate the lenses; in those cases the

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21. Some will disagree with the exclusion of cases of this category from the group with improved vision. If the bulk of opinion approves the objection, the classification can be modified to include these cases as another group or subgroup (slight improvement). The number of cases eligible for such a group, however, does not appear to substantiate its necessity; in the present series of 165 cases, only 5 (table 10) would fall into that category.

22. Cases in which the follow-up was definitely terminated, as by enucleation or a second corneal transplantation, were included in the analysis, regardless of the follow-up period.

visual acuity with the contact lenses was disregarded. The length of the follow-up period in the seventh column is given to the nearest whole month. The comments under "Clarity of Graft" are taken from the patient's record. The last column ("Final Visual Acuity") is my evaluation of the success of the operation, according to the standards already outlined.

*Keratoconus.*—Thirty-five corneal transplantations were performed on 26 patients with conical cornea. The results in this group of operations are shown in table 2. Preoperative visual acuity was better than 20/200 in 7 eyes and varied from counting fingers to 20/200 in the remaining 28 eyes. Postoperative visual acuity was improved (better than 20/200) in 10 eyes, unchanged (no significant change) in 13 eyes and decreased in 12 eyes. Total loss of vision occurred in 1 instance (operation 25). All 10 eyes with improved vision had preoperative vision of 20/200 or less. Eight of these 10 eyes required high minus correction after operation to obtain the improved visual acuity; the remaining 2 eyes showed moderately high hypermetropia and mixed astigmatism. Only 1 of the 10 eyes attained better than 20/200 visual acuity without correction (operation 8). Vision was not improved in any of the 7 eyes with better than 20/200 visual acuity before operation; 6 eyes in this group showed loss of vision, and the remaining eye showed no significant change.

With respect to transparency of the graft, 18 eyes showed permanently clear transplants (average follow-up period, forty-seven months); 6 eyes, cloudy grafts, and 11 eyes, opaque grafts. The difference between the number of clear grafts and the number of eyes with improved vision is noteworthy. Only 9 of the eyes with clear transplants showed improved vision. In 1 eye (operation 35) visual acuity was improved in the presence of a cloudy graft. Figure 1 is a photograph, taken nine years after operation, of a clear graft (operation 4) without improvement in vision.

The follow-up period for the group averaged 32.5 months. The difference between the length of the follow-up period for operation 1 (one hundred and thirty-four months) and that for operation 2 (ten months) on the same patient occurred because operation 2 was followed by a second transplantation ten months later. A second transplantation also explains the brevity of the follow-up period for 7 other operations in this group.

Eleven of the patients with conical cornea had multiple operations. Nine patients had a corneal transplantation on each eye. Four of these patients with bilateral transplantations and 2 patients with unilateral grafts had secondary corneal transplantations. In the group with bilateral grafts, 1 patient obtained improved visual acuity in both eyes;

TABLE 2.—Results of Corneal Transplantation in Cases of Keratoconus

Year	Operation No.	Clinic No.	Age	Sex	Preoperative Visual Acuity and Refraction	Postoperative Visual Acuity and Refraction	Length of Follow-Up Period, Mo.	Clarity of Graft	Final Visual Acuity
1937	1	509103	30	M	3/200; no improvement with lenses	20/27 with — 12.00 sph. C — 6.50 cyl., axis 5	134	Clear	Improved *
	2	509103	30	M	5/200; no improvement with lenses	Count fingers; no improvement with lenses	10†	Cloudy	Unchanged‡
1938	3	543635	40	M	Count fingers; no improvement with lenses	6/200 with — 18.00 sph. C — 3.50 cyl., axis 110	50	Clear	Unchanged
	4	560902	11	M	Count fingers; no improvement with lenses	2/200 with — 19.00 sph. C — 3.00 cyl., axis 150	108	Clear	Unchanged
1939	5	543603	25	M	3/200; no improvement with lenses	20/50 with — 13.00 sph. C — 4.50 cyl., axis 180	6	Clear	Improved
	6	508397	24	M	3/200; 20/50 with contact lens	Count fingers; no improvement with lenses	74†	Clear	Loss of vision§
1940	7	560902	12	M	8/200 with lenses; refraction unknown	Hand movements; no improvement with lenses	6†	Opaque	Loss of vision
	8	604252	22	M	20/200; refraction unknown	20/50 with — 8.50 sph. C — 2.50 cyl., axis 90	67	Clear	Improved
1941	9	604252	22	M	20/70; refraction unknown	8/200 with — 6.50 sph.	63	Clear	Loss of vision
	10	508397	30	M	8/200; 20/50 with contact lens	Count fingers; no improvement with lenses	72	Clear	Loss of vision
1942	11	448027	31	M	Count fingers; no improvement with lenses	20/30 with — 7.50 sph. C — 3.00 cyl., axis 10	48	Clear	Improved
	12	692638	21	M	2/200; no improvement with lenses	Hand movements; no improvement with lenses	24	Opaque	Loss of vision
1943	13	644667	29	M	Count fingers; no improvement with lenses	Hand movements; no improvement with lenses	24†	Opaque	Unchanged
	14	448027	32	M	20/30 with lenses; refraction unknown	20/40 with — 13.00 sph. C — 3.00 cyl., axis 65	36	Clear	Unchanged
	15	604321	27	F	Count fingers; refraction unknown	Count fingers; no improvement with lenses	56	Opaque	Unchanged
1944	16	689040	40	F	3/200; no improvement with lenses	Hand movements; no improvement with lenses	25	Opaque	Loss of vision
	17	729178	20	M	5/200; no improvement with lenses	20/30 with + 4.50 sph. C + 3.00 cyl., axis 110	13	Clear	Improved
	18	745918	30	F	20/200; no improvement with lenses	20/50 with — 11.50 sph. C — 7.00 cyl., axis 25	48	Clear	Improved
	19	747056	41	F	20/100 with lenses; refraction unknown	2/200; no improvement with lenses	9	Cloudy	Loss of vision
	20	729178	21	M	20/20 with correction of + 3.75 D., axis 80 (20/40 without corr.)	20/70; no improvement with lenses	7	Clear	Loss of vision
1945	21	620314	25	M	8/200; no improvement with lenses	Hand movements; no improvement with lenses	13	Opaque	Loss of vision
	22	756609	43	F	Count fingers; no improvement with lenses	Count fingers; no improvement with lenses	11	Cloudy	Unchanged
	23	756188	42	F	2/200; no improvement with lenses	7/200 with — 2.00 sph. C — 7.00 cyl., axis 120	29	Clear	Unchanged
	24	805184	26	M	Count fingers; no improvement with lenses	20/30 with — 8.00 sph. C — 4.50 cyl., axis 105	27	Clear	Improved
1946	25	812239	33	F	Count fingers; no improvement with lenses	No light perception	22	Opaque	Loss of all vision
	26	813875	35	M	20/100 with contact lens (well tolerated)	Hand movements; no improvement with lenses	9†	Opaque	Loss of vision
	27	791725	44	F	Count fingers; no improvement with lenses	Count fingers; no improvement with lenses	29†	Clear	Unchanged
	28	817600	25	F	15/200; no improvement with lenses	20/50 with + 1.50 sph. C — 4.00 cyl., axis 25	9	Clear	Improved
	29	753416	31	F	Count fingers; no improvement with lenses	Hand movements; no improvement with lenses	16	Opaque	Unchanged
	30	745918	31	F	10/200; no improvement with lenses	20/100 with — 10.00 sph. C — 7.00 cyl., axis 120	24	Clear	Improved
	31	841715	21	M	Count fingers; no improvement with lenses	Count fingers; no improvement with lenses	8	Cloudy	Unchanged
	32	791725	45	F	Count fingers; no improvement with lenses	Hand movements; no improvement with lenses	24†	Cloudy	Unchanged
	33	805184	27	M	10/200; no improvement with lenses	Light perception; no improvement with lenses	15†	Opaque	Loss of vision
	34	847561	29	F	5/200; no improvement with lenses	Count fingers; no improvement with lenses	7	Opaque	Unchanged
1947	35	858475	19	F	10/200 with — 16.00 sph. C — 8.00 cyl., axis 180	20/100 with — 5.50 sph. C — 3.00 cyl., axis 155	14	Cloudy	Improved

\* Final visual acuity was improved to better than 20/200.

† Followed by a second corneal transplantation.

‡ No significant change in visual acuity occurred.

§ Final visual acuity was decreased more than one step in the visual scale.

2 patients, improved visual acuity in one eye and no significant change in the other, and 3 patients, improved visual acuity in one eye and a loss of vision in the other eye. Of the 3 remaining patients, 1 had bilateral loss of vision, 1 had no significant change in either eye and 1 had a loss of vision in one eye with no significant change in the other. The secondary transplantations, therefore, resulted in improvement in vision in 2 instances.



Fig. 1.—Photograph, taken nine years after operation, of a clear corneal transplant (operation 4) without improvement in vision. Before operation vision was reduced by keratoconus to counting fingers; postoperative visual acuity was limited to perception of hand movements, correctable to 2/200 with a high minus lens.

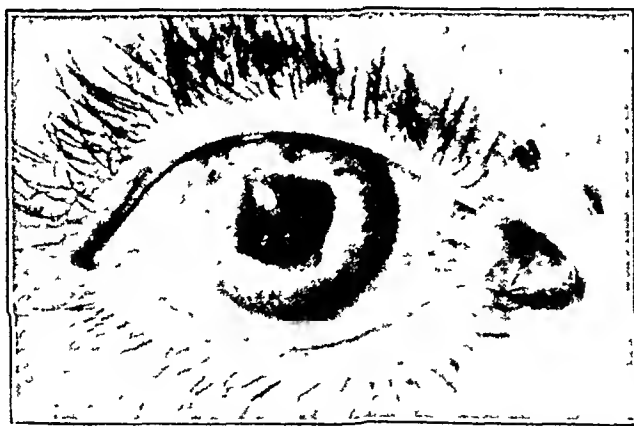


Fig. 2.—Photograph, one year after operation, of a clear corneal transplant (operation 36) without significant improvement in vision. Before operation familial corneal dystrophy reduced this patient's vision to perception of hand movements. Postoperative visual acuity was corrected to 20/50 for nearly a year, when the cornea began to bulge forward, causing steadily increasing myopia and reduction in vision. Sixteen months after operation visual acuity was improved to 12/200 with a high minus lens only with difficulty.

*Corneal Dystrophies.*—Thirteen corneal transplantations were performed on 13 patients with corneal dystrophy. There were 3 eyes with Haab-Dimmer lattice dystrophy, 1 eye with Groenouw's nodular



dystrophy, 1 eye with Fuchs's epithelial dystrophy<sup>23</sup> and 8 eyes with unclassified dystrophies. The results are shown in table 3. Before operation visual acuity was less than 20/200 in all 13 eyes. After operation visual acuity was improved in 2 eyes, unchanged in 7 eyes and decreased in 4 eyes. There was loss of all light perception in 2 eyes. The 2 improved eyes each obtained visual acuity of 20/100, with moderately high myopic correction. Four eyes had clear grafts; 2, cloudy grafts, and 7, opaque grafts. Figure 2 is a photograph of one of the

TABLE 3.—Results of Corneal Transplantation in Cases of Corneal Dystrophy

Year	Operation No.	Clinic No.	Age	Sex	Preoperative Visual Acuity and Refraction	Postoperative Visual Acuity and Refraction	Length of Follow-Up Period, Mo.	Clarity of Graft	Final Visual Acuity
Haas-Dimmer Type									
1947	36	858147	32	F	Hand movements; no improvement with lenses	12/200 with — 9.00 sph. $\odot$ — 6.00 cyl., axis 105	16	Clear	Unchanged
	37	860406	35	F	2/200; no improvement with lenses	No light perception	15	Opaque	Loss of all vision
	38	861191	61	M	4/200; no improvement with lenses	20/100 with — 5.50 sph. $\odot$ — 1.50 cyl., axis 100	14	Clear	Improved
Groenouw's Type									
1946	39	833160	42	F	Hand movements; no improvement with lenses	20/100 with — 4.00 sph. $\odot$ — 8.00 cyl., axis 160	8	Clear	Improved
Fuch's Epithelial Type									
1938	40	561773	55	M	4/200; no improvement with lenses	Light perception; no improvement with lenses	12*	Opaque	Loss of vision
Unclassified									
1945	41	772717	44	M	20/200 with lenses; refraction unknown	6/200 with — 9.00 sph. $\odot$ — 1.50 cyl., axis 165	24	Clear	Unchanged
1946	42	803631	59	F	10/200; refraction unknown	5/200; no improvement with lenses	11	Opaque	Unchanged
	43	847505	68	F	Count fingers; no improvement with lenses	No light perception	20	Opaque	Loss of all vision
	44	843156	29	M	Count fingers; no improvement with lenses	Hand movements; no improvement with lenses	15	Cloudy	Unchanged
	45	847257	33	F	10/200; no improvement with lenses	Light perception; no improvement with lenses	14*	Opaque	Loss of vision
	46	826724	24	F	3/200; no improvement with lenses	15/200 with — 10.00 sph.	11	Cloudy	Unchanged
	47	855524	20	M	3/200; no improvement with lenses	8/200 with — 11.00 sph.	16	Opaque	Unchanged
	48	884815	50	F	Count fingers; no improvement with lenses	Hand movements; no improvement with lenses	10	Opaque	Unchanged

\* Followed by a second corneal transplantation.

clear grafts (operation 36) without improvement in vision. The patient had 20/50 vision, with high myopic correction, for approximately one year after operation, when the graft began to bulge outward, as in conical cornea, with rapid loss of visual acuity. The follow-up period for this group averaged 14.3 months. Two patients in this group of dystrophies had secondary corneal transplantations, neither of which resulted in improvement.

23. Fuchs's epithelial dystrophy should not be considered with the other types of dystrophy in this category. The operation for this condition was included in this group because a single case did not appear to justify separate classification.

*Interstitial Keratitis.*—Twenty-one corneal transplantations were performed on 17 patients with interstitial keratitis. The results of these operations are shown in table 4. Preoperative visual acuity was better than 20/200 in 2 eyes and varied from light perception to 20/200 in the remaining 19 eyes. After operation, visual acuity was improved in 3 eyes and was unchanged in 11 eyes, and there was a decrease of vision in 7 eyes. Loss of all light perception occurred in 1 eye (operation 49). Two of the 3 eyes with postoperative visual acuity of better than 20/200 required modest correction for hypermetropia, while the third eye required a high myopic lens. The grafts remained clear in 5 eyes, became cloudy in 4 eyes and became opaque in 10 eyes. One eye was enucleated four days after transplantation because of panophthalmitis, and the graft became detached in 1 eye. Figure 3 is a photograph of a clear graft (operation 59) associated with a loss of

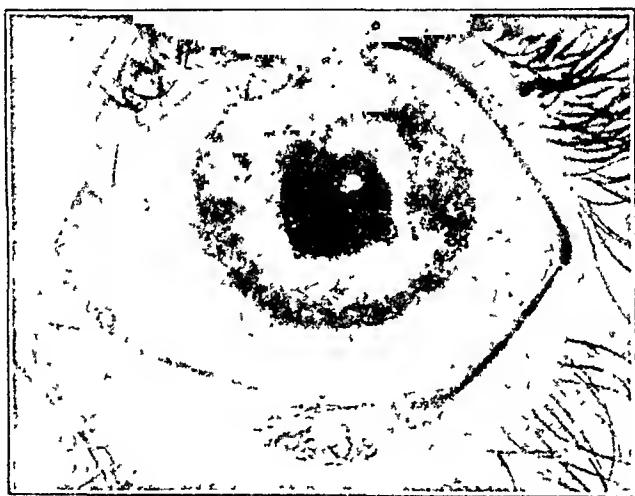


Fig. 3.—Photograph of a clear corneal transplant (operation 59) with loss of visual acuity. Before operation visual acuity was reduced to 20/100 by interstitial keratitis; postoperative visual acuity was reduced to counting fingers and was not improved with lenses.

vision. Before operation this patient had 20/100 visual acuity in this eye with correction; seven years after operation, although the graft remained perfectly clear, vision was limited to counting fingers and there was no improvement with lenses. The follow-up period for these 21 operations averaged 33.3 months. Eight patients in this group had secondary corneal transplantations, none of which was successful.

*Chemical Burns.*—Nine corneal transplantations were performed on 7 patients with chemical burns of the cornea. Three of these patients suffered acid burns; 2, alkaline burns, and the remaining 2, chemical burns of uncertain nature. The results of these corneal transplantations are shown in table 5. Preoperative visual acuity was less than 20/200 in all 9 eyes: Vision in 4 eyes was limited to counting fingers, in 3 eyes to light perception and in 1 eye to perception of hand movements,

TABLE 4.—Results of Corneal Transplantation in Cases of Interstitial Keratitis

Year	Operation No.	Clinic No.	Age	Sex	Preoperative Visual Acuity and Refraction	Postoperative Visual Acuity and Refraction	Length of Follow-Up Period, Mo.	Clarity of Graft	Final Visual Acuity
1933	49	329859	69	M	6/200; no improvement with lenses	No light perception (enucleation 4 days post-operatively)	4	.....	Loss of all vision
1935	50	441489	39	M	20/200; no improvement with lenses	Light perception; no improvement with lenses	4*	.....	Loss of vision
	51	359963	25	M	Count fingers; no improvement with lenses	Count fingers; no improvement with lenses	7	Clear	Unchanged
1936	52	497487	19	F	Light perception; no improvement with lenses	Light perception; no improvement with lenses	120	Cloudy	Unchanged
	53	497487	19	F	Count fingers; no improvement with lenses	5/200; no improvement with lenses	22*	Cloudy	Unchanged
1937	55	489940	38	F	20/70 with — 3.50 sph. $\odot$ — 1.50 cyl., axis 90	Count fingers; no improvement with lenses	4*	Cloudy	Loss of vision
	54	489940	38	F	20/200 with — 3.50 sph.	20/70 with — 12.00 sph.	6	Clear	Improved
1939	56	789539	22	F	3/200; no improvement with lenses	Hand movements; no improvement with lenses	98	Opaque	Loss of vision
	57	594229	32	M	20/200 with + 1.00 sph. $\odot$ + 5.00 cyl., axis 180	Hand movements; no improvement with lenses	18*	Opaque	Loss of vision
1941	58	633231	24	M	Hand movements; no improvement with lenses	Count fingers; no improvement with lenses	90	Opaque	Unchanged
	59	610734	48	F	20/100 with — 4.00 sph.	Count fingers; no improvement with lenses	89*	Opaque	Loss of vision
	60	633231	24	M	Hand movements; no improvement with lenses	Hand movements; no improvement with lenses	42*	Opaque	Unchanged
1942	61	646646	40	F	2/200; no improvement with lenses	Count fingers; no improvement with lenses	20	Opaque	Unchanged
1944	62	766136	27	M	Count fingers; no improvement with lenses	20/30 with + 2.00 cyl., axis, 135	32	Clear	Improved
	63	766136	27	M	10/200; no improvement with lenses	20/50 with + 2.00 sph. $\odot$ + 2.25 cyl., axis 45	31	Clear	Improved
1945	64	756598	56	M	Count fingers; no improvement with lenses	3/200 with + 10.00 sph. $\odot$ + 6.00 cyl., axis 65	42	Opaque	Unchanged
	65	782144	29	M	5/200 with — 20.00 sph.	Count fingers; no improvement with lenses	14*	Opaque	Unchanged
1946	66	654502	15	F	Count fingers; no improvement with lenses	Light perception; no improvement with lenses	22*	Opaque	Loss of vision
	67	834570	26	F	10/200; no improvement with lenses	Count fingers; no improvement with lenses	18	Cloudy	Unchanged
	68	833467	28	F	Hand movements; no improvement with lenses	Hand movements; no improvement with lenses	6	Opaque	Unchanged
1947	69	865196	21	F	20/200; refraction unknown	10/200; no improvement with lenses	15	Clear	Unchanged

\* Followed by a second corneal transplantation.

TABLE 5.—Results of Corneal Transplantation in Cases of Chemical Burns

Year	Operation No.	Clinic No.	Age	Sex	Preoperative Visual Acuity and Refraction	Postoperative Visual Acuity and Refraction	Length of Follow-Up Period, Mo.	Clarity of Graft	Final Visual Acuity
1933	70	365895	40	M	5/200; no improvement with lenses	Count fingers; no improvement with lenses	14*	Opaque	Unchanged
1934	71	466643	22	M	Hand movements; no improvement with lenses	Hand movements; no improvement with lenses	26*	Cloudy	Unchanged
1935	72	442672	26	M	Light perception; no improvement with lenses	No light perception	8	Opaque	Loss of all vision
	73	457018	22	M	Light perception; no improvement with lenses	Light perception; no improvement with lenses	43*	Opaque	Unchanged
	74	458682	23	M	Count fingers; no improvement with lenses	Count fingers; no improvement with lenses	47*	Opaque	Unchanged
	75	458682	23	M	Count fingers; no improvement with lenses	Count fingers; no improvement with lenses	8*	Opaque	Unchanged
	76	441982	26	M	Light perception; no improvement with lenses	Light perception; no improvement with lenses	1	.....	Unchanged
1938	77	875514	31	M	Count fingers; no improvement with lenses	Light perception; no improvement with lenses	120	Opaque	Loss of vision
	78	875514	31	M	Count fingers; no improvement with lenses	Count fingers; no improvement with lenses	8*	Opaque	Unchanged

\* Period followed by second corneal transplantation.

TABLE 6.—Results of Corneal Transplantation in Cases of Traumatic Scars

Year	Operation No.	Clinic No.	Age	Sex	Preoperative Visual Acuity and Refraction	Postoperative Visual Acuity and Refraction	Length of Follow-Up Period, Mo.	Clarity of Graft	Final Visual Acuity
1934	79	346693	22	F	Light perception; no improvement with lenses	Hand movements; no improvement with lenses	144	Opaque	Unchanged
1935	80	454248	55	F	8/200; no improvement with lenses	Hand movements; no improvement with lenses	10	Opaque	Loss of vision
1937	81	514299	29	M	6/200; no improvement with lenses	10/200 with + 9.00 sph.	61	Clear	Unchanged
1944	82	752341	26	M	5/200; no improvement with lenses	Count fingers; no improvement with lenses	46	Opaque	Unchanged
1945	83	603599	41	M	20/200; no improvement with lenses	20/70 with — 0.50 sph. $\odot$ — 4.00 cyl., axis 130	39	Clear	Improved
	84	789971	36	M	20/40 with + 3.50 sph.	20/200 (improved to 20/20 with a very high correction, but patient could not wear it)	13	Clear	Loss of vision

TABLE 7.—Results of Corneal Transplantation in Cases with Postinflammatory Scars

Year	Operation No.	Clinic No.	Age	Sex	Preoperative Visual Acuity and Refraction	Postoperative Visual Acuity and Refraction	Length of Follow-Up Period, Mo.	Clarity of Graft	Final Visual Acuity
1933	85	324378	55	F	Hand movements; no improvement with lenses	Light perception; no improvement with lenses	25	Opaque	Unchanged
	86	411857	20	M	Count fingers; no improvement with lenses	Count fingers; no improvement with lenses	15*	Cloudy	Unchanged
1935	87	455825	16	M	Hand movements; no improvement with lenses	Hand movements; no improvement with lenses	27	Opaque	Unchanged
1936	88	371425	24	M	Hand movements; no improvement with lenses	Hand movements; no improvement with lenses	27*	Cloudy	Unchanged
	89	487454	35	M	20/200; no improvement with lenses	Hand movements; no improvement with lenses	12*	Opaque	Loss of vision
1937	90	522939	45	M	Hand movements; no improvement with lenses	Light perception; no improvement with lenses	27	Opaque	Unchanged
	91	847335	26	F	Hand movements; no improvement with lenses	Hand movements; no improvement with lenses	12*	Cloudy	Unchanged
1938	92	406036	30	M	10/200; no improvement with lenses	20/200 with — 1.00 sph. $\odot$ + 9.00 cyl., axis 70	102	Clear	Unchanged
	93	558409	13	F	10/200; no improvement with lenses	20/70 with — 3.50 sph.	80	Clear	Improved
	94	561434	29	F	Hand movements; no improvement with lenses	No light perception	115	Opaque	Loss of all vision
1939	95	590851	24	F	Light perception; no improvement with lenses	No light perception	36	Opaque	Loss of all vision
1940	96	565344	5	M	Light perception; no improvement with lenses	Light perception; no improvement with lenses	10*	Opaque	Unchanged
	97	568702	6	M	Hand movements; no improvement with lenses	12/200; no improvement with lenses	96	Clear	Unchanged
	98	332408	13	F	10/200; no improvement with lenses	No light perception (enucleation)	2	Opaque	Loss of all vision
	99	617664	18	F	20/200; no improvement with lenses	Hand movements; no improvement with lenses	36	Clear	Loss of vision
1941	100	624147	23	M	20/50 with — 0.50 sph.	Hand movements; no improvement with lenses	38*	Opaque	Loss of vision
	101	533789	47	M	Hand movements; no improvement with lenses	No light perception	13	Opaque	Loss of all vision
1944	102	609653	55	F	Count fingers; no improvement with lenses	Count fingers; no improvement with lenses	11	Cloudy	Unchanged
1945	103	770061	37	F	Hand movements; no improvement with lenses	3/200; no improvement with lenses	13	Cloudy	Unchanged
1947	104	824446	35	F	Hand movements; no improvement with lenses	Hand movements; no improvement with lenses	18	Opaque	Unchanged
	105	827386	27	F	20/70; no improvement with lenses	20/200; no improvement with lenses	9	Cloudy	Loss of vision
	106	878080	22	M	5/200; no improvement with lenses	20/40 with — 0.50 sph. $\odot$ + 2.50 cyl., axis 75	9	Clear	Improved

\* Followed by second corneal transplantation.

and in 1 eye visual acuity was 5/200. In none of these eyes was postoperative visual acuity improved to better than 20/200. In 7 eyes there was no significant change in vision, and 2 eyes showed a loss of vision. There were no transparent grafts in this series. One graft became cloudy, and 7 grafts became opaque; 1 transplant was detached and lost. The average follow-up period for the group was 30.5 months. Five of these patients with chemical burns had multiple operations; 2 had corneal transplantations on both eyes, and all 5 had secondary corneal transplantations. Two patients had 4 grafts (2 on each eye), and 1 patient (operation 71) had 4 grafts on one eye. None of the 9 secondary transplantations resulted in improvement of vision. Three of the latter operations resulted in loss of light perception.

*Traumatic Scars.*—Six corneal transplantations were performed on 6 patients with corneal scars resulting from trauma. The results in these cases are shown in table 6. Preoperative visual acuity was 20/200 or less in 5 eyes and 20/40, with correction, in 1 eye. Postoperative visual acuity was improved in 1 eye; there was no significant change in visual acuity in 3 eyes, and there was loss of vision in 2 eyes. There were clear transplants in 3 eyes and opaque transplants in 3 eyes. The follow-up period for the group averaged 52.1 months. There were no secondary transplantations in these cases.

*Postinflammatory Scars.*—Twenty-two corneal transplants were performed on 22 patients with corneal lesions following a definite inflammatory process. The inflammations given in the histories of these patients were as follows:

	No. of Cases
Corneal ulcer.....	4
Diphtheria .....	2
Trachoma .....	1
Ophthalmia neonatorum .....	1
Gonorrheal infection in the adult.....	1
Corneal abscess .....	1
Measles .....	1
Inflammation of uncertain cause.....	11
Total .....	22

The pertinent data in this series of operations are shown in table 7. Preoperative visual acuity was better than 20/200 in 2 eyes and varied from light perception to 20/200 in the remaining 20 eyes. Postoperative visual acuity was improved in 2 eyes, to 20/40 in 1 case and to 20/70 in the other; both eyes required myopic correction to attain this acuity. There was no significant change in vision in 12 eyes, and a loss of vision occurred in 8 eyes, with loss of light perception in 4 of these 8 eyes. There were clear transplants in 5 eyes, cloudy transplants

in 6 eyes and opaque transplants in 11 eyes. Figure 4 is a photograph of the clear graft (operation 99) associated with a decrease in vision. Visual acuity in this eye was 20/200 before operation and was limited to perception of hand movements after transplantation. The follow-up period for the group averaged 33.3 months. Six patients had secondary corneal transplantations, none of which resulted in improved vision.



Fig. 4.—Photograph of a clear corneal transplant (operation 99) associated with loss of vision. Before operation a corneal leukoma reduced visual acuity to 20/200; after operation visual acuity was reduced to perception of hand movements and was not improved with lenses.

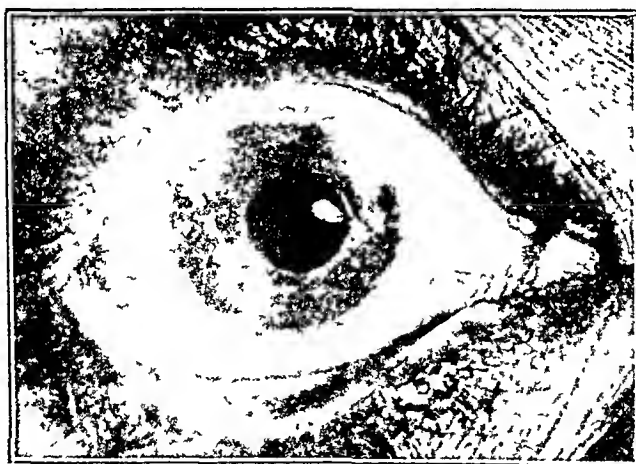


Fig. 5.—Photograph, taken fourteen months after operation, of a clear corneal transplant (operation 118) with improved vision. Before operation corneal leukomas of unknown origin reduced this patient's vision to perception of hand movements in each eye. After a transplant on each eye, visual acuity with correction was 20/50 in each eye.

7. *Corneal Scars of Unknown Origin.*—Twenty-four corneal transplantations were performed on 19 patients with corneal scars but without a definite history of ocular disease or injury. It is likely that many of these scars belonged in the preceding (postinflammatory) group. Also included in this category are the following miscellaneous conditions: primary fatty degeneration of the cornea. 1 case; band keratitis,

1 case; a descemetoele, 1 case, and Hurler's syndrome (lipochondrodystrophy), 1 case. The results in this group of assorted cases are shown in table 8. Preoperative visual acuity was 20/40 and 20/70 in

TABLE 8.—Results of Corneal Transplantation Cases with Scars of Unknown Cause

Year	Operation No.	Clinic No.	Age	Sex	Preoperative Visual Acuity and Refraction	Postoperative Visual Acuity and Refraction	Length of Follow-Up Period, Mo.	Clarity of Graft	Final Visual Acuity
1934	107	759738	58	F	Hand movements; no improvement with lenses	Count fingers; no improvement with lenses	168	Opaque	Unchanged
	108	759738	58	F	4/200; no improvement with lenses	5/200; no improvement with lenses	44*	Opaque	Unchanged
1935	109	439832	21	M	Count fingers; no improvement with lenses	Count fingers; no improvement with lenses	14*	Opaque	Unchanged
1936	110	488464	60	M	3/200; no improvement with lenses	Count fingers; no improvement with lenses	72	Cloudy	Unchanged
	111	470986	24	M	Light perception; no improvement with lenses	No light perception	49	Opaque	Loss of all vision
	112	488464	60	M	20/70; no improvement with lenses	10/200; no improvement with lenses	72	Cloudy	Loss of vision
1937	113	509661	41	F	Hand movements; no improvement with lenses	Hand movements; no improvement with lenses	34*	Opaque	Unchanged
	114	509661	41	F	Count fingers; no improvement with lenses	Count fingers; no improvement with lenses	33*	Opaque	Unchanged
	115	516335	48	F	Hand movements; no improvement with lenses	20/50 with + 4.00 sph. C + 1.00 cyl., axis 120	48	Clear	Improved
	116	524033	44	F	5/200; no improvements with lenses	10/200; no improvement with lenses	10	Cloudy	Unchanged
	117	459169	41	F	Count fingers; no improvement with lenses	Light perception; no improvement with lenses	95	Opaque	Loss of vision
	118	516335	48	F	Hand movements; no improvement with lenses	20/50 with + 1.00 sph.	45	Clear	Improved
	119	519674	20	M	10/200; no improvement with lenses	Hand movements; no improvement with lenses	42	Cloudy	Loss of vision
1938	120	542880	11	M	Hand movements; no improvement with lenses	Hand movements; no improvement with lenses	110	Opaque	Unchanged
1939	121	573504	44	M	15/200; no improvement with lenses	Light perception; no improvement with lenses	5*	Cloudy	Loss of vision
1941	122	643388	45	M	5/200; no improvement with lenses	No light perception	82	Opaque	Loss of all vision
1942	123	627786	28	F	15/200; no improvement with lenses	20/200; no improvement with lenses	72	Cloudy	Unchanged
1944	124	764672	35	F	6/200; no improvement with lenses	10/200; no improvement with lenses	15*	Cloudy	Unchanged
1945	125	764287	56	F	Count fingers; no improvement with lenses	Light perception; no improvement with lenses	10	Cloudy	Loss of vision
Primary Fatty Degeneration of Cornea									
1939	126	557042	39	M	20/200; no improvement with lenses	Count fingers; no improvement with lenses	108	Opaque	Loss of vision
	127	557042	39	M	20/200; no improvement with lenses	Count fingers; no improvement with lenses	41*	Opaque	Loss of vision
Band Keratitis									
1945	128	752428	52	F	3/200 with — 3.25 sph.	5/200 with — 10.00 sph.	40	Clear	Unchanged
Descemetoele									
	129	867895	32	F	20/40; no refraction	3/200; no improvement with lenses	25	Clear	Loss of vision
Hurler's Syndrome									
1948	130	895612	18	M	2/200; no improvement with lenses	No light perception (enucleation)	1	.....	Loss of all vision

\* Followed by another corneal transplantation.

2 eyes and ranged from 20/200 to light perception in the remaining 22 eyes. After operation, visual acuity was improved in 2 eyes, unchanged in 11 eyes and decreased in 11 eyes. Three eyes in the last group showed complete loss of vision. The 2 successful opera-

tions (115 and 118) were performed on the same patient. In this patient, preoperative vision was equal to perception of hand movements in each eye, not improved with lenses; postoperative visual acuity was 20/50 in each eye, with hypermetropic correction. Figure 5 is a photograph of the patient's right eye after operation. There were 4 clear grafts, 8 cloudy grafts and 11 opaque grafts in this series of operations; 1 graft became detached, and the eye was enucleated. The follow-up period for these patients averaged 51.8 months. Eight patients

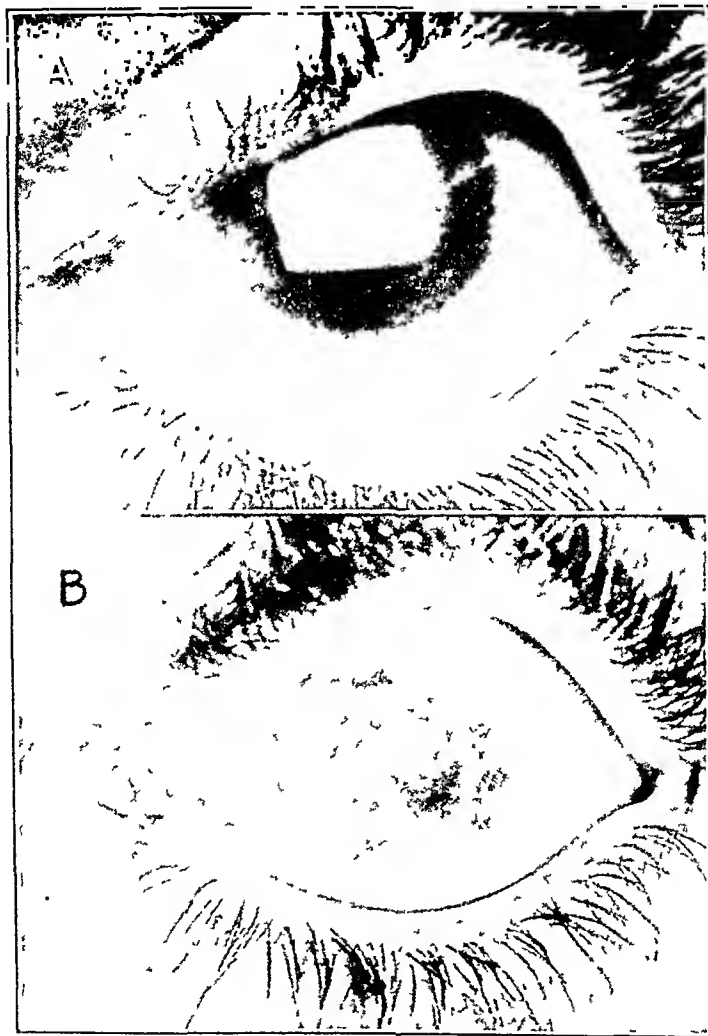


Fig. 6.—Photographs showing a clear secondary corneal transplant. *A*, photograph, six months after operation, of the result of the initial operation on that eye (operation 7); vision was then limited to perception of hand movements and was not improved with lenses. *B*, photograph, seven months after operation, showing result of the second transplantation; visual acuity was then improved to 20/50 with a very high minus lens.

had multiple corneal transplantations. Five patients had a corneal transplantation on each eye, and 6 patients had 7 secondary corneal transplantations, none of which was successful.

8. *Secondary Corneal Transplantations.*—Thirty-five corneal transplantations were performed on 32 eyes on which one or more corneal transplantations had already been done. (There were 5 additional sec-



TABLE 9.—Results in Secondary Corneal Transplantation

Year	Operation No.	Clinic No.	Age	Sex	Preoperative Visual Acuity and Refraction	Postoperative Visual Acuity and Refraction	Length of Follow-Up Period, Mo.	Clarity of Graft	Final Visual Acuity
1934	131	365895	41	M	Count fingers; no improvement with lenses	No light perception	39	Opaque	Loss of all vision
1935	132	441849	39	M	Hand movements; no improvement with lenses	Hand movements; no improvement with lenses	60	Opaque	Unchanged
	133	411857	21	M	Count fingers; no improvement with lenses	Hand movements; no improvement with lenses	51	Cloudy	Unchanged
1936	134	458682	24	M	Count fingers; no improvement with lenses	Hand movements; no improvement with lenses	88	Opaque	Unchanged
	135	439532	21	M	Count fingers; no improvement with lenses	No light perception	7	Opaque	Loss of all vision
	136	466643	22	M	Hand movements; no improvement with lenses	Hand movements; no improvement with lenses	8*	Cloudy	Unchanged
1937	137	466643	23	M	Hand movements; no improvement with lenses	Hand movements; no improvement with lenses (third transplant)	9*	Cloudy	Unchanged
	138	759738	58	F	5/200; no improvement with lenses	Hand movements; no improvement with lenses	133	Opaque	Loss of vision
	139	487454	37	M	Hand movements; no improvement with lenses	No light perception	17	Opaque	Loss of all vision
	140	466643	23	M	Hand movements; no improvement with lenses	No light perception (enucleation; 4th transplant)	43	Opaque	Loss of all vision
1938	141	509103	30	M	Count fingers; no improvement with lenses	Light perception; no improvement with lenses	117	Cloudy	Loss of vision
	142	371426	28	M	Hand movements; no improvement with lenses	Light perception; no improvement with lenses	30	Clear	Unchanged
	143	497457	20	F	5/200; no improvement with lenses	5/200; no improvement with lenses	99	Cloudy	Unchanged
	144	847335	27	F	Hand movements; no improvement with lenses	No light perception	96	Opaque	Loss of all vision
	145	875514	31	M	Hand movements; no improvement with lenses	Hand movements; no improvement with lenses	6*	Opaque	Unchanged
1939	146	457018	25	M	Light perception; no improvement with lenses	Light perception; no improvement with lenses	111	Opaque	Unchanged
	147	458682	27	M	Count fingers; no improvement with lenses	Hand movements; no improvement with lenses	50	Opaque	Unchanged
	148	875514	31	M	Hand movements; no improvement with lenses	No light perception (3d transplant)	105	Opaque	Loss of all vision
	149	489340	38	F	Count fingers; no improvement with lenses	20/200; no improvement with lenses	15	Clear	Unchanged
	150	561773	56	M	Light perception; no improvement with lenses	Hand movements; no improvement with lenses	70	Cloudy	Unchanged
	151	573564	44	M	Count fingers; no improvement with lenses	Light perception; no improvement with lenses	34	Opaque	Loss of vision
1940	152	560002	13	M	Hand movements; no improvement with lenses	20/50 with —20.00 sph. C —3.00 cyl., axis 40	49	Clear	Improved
	153	565344	6	M	Light perception; no improvement with lenses	Hand movements; no improvement with lenses	63	Clear	Unchanged
1941	154	594299	33	M	Hand movements; no improvement with lenses	Count fingers; no improvement with lenses	79	Cloudy	Unchanged
1943	155	557042	42	M	Count fingers; no improvement with lenses	Count fingers; no improvement with lenses	63	Opaque	Unchanged
1944	156	624147	28	M	Hand movements; no improvement with lenses	Hand movements; no improvement with lenses	7	Opaque	Unchanged
	157	633231	27	M	Hand movements; no improvement with lenses	Hand movements; no improvement with lenses	44	Opaque	Unchanged
1945	158	644607	31	M	Hand movements; no improvement with lenses	Count fingers; no improvement with lenses	44	Opaque	Unchanged
	159	808397	35	M	Count fingers; no improvement with lenses	20/70 with —4.00 sph. C —1.25 cyl., axis 50	20	Clear	Improved
1946	160	764072	36	F	10/200; no improvement with lenses	4/200; no improvement with lenses	23	Cloudy	Unchanged
	161	813875	56	M	Hand movements; no improvement with lenses	No light perception	11	Opaque	Loss of all vision
	162	782144	30	M	Count fingers; no improvement with lenses	No light perception (enucleation)	4	Opaque	Loss of all vision
1947	163	610734	52	F	Count fingers; no improvement with lenses	Count fingers; no improvement with lenses	9	Cloudy	Unchanged
	164	654802	17	F	Light perception; no improvement with lenses	7/200; no improvement with lenses	7	Opaque	Unchanged
	165	805184	28	M	Light perception; no improvement with lenses	Light perception; no improvement with lenses	6	Opaque	Unchanged

\* Followed by a third corneal transplantation.

ondary operations among the cases excluded for lack of a six months' follow-up.) The initial lesions in these 32 eyes before the first corneal transplantation were as follows:

	No. of Eyes
Keratoconus .....	6
Corneal dystrophy .....	1
Interstitial keratitis .....	8
Chemical burns .....	6
Postinflammatory scars .....	6
Scars of unknown etiology .....	5
Total .....	32

After the first corneal transplantation, the pathologic process in these eyes had little in common with these lesions. After operation the corneas, for the most part, showed extensive vascularization and opacification, and the majority of the eyes had secondary glaucoma. Therefore, because they resembled each other more than anything else, these eyes have been grouped together in this separate division. The data on these secondary operations are shown in table 9. Preoperative vision in these eyes ranged from light perception to 10/200. After operation, 2 eyes showed improved visual acuity, 1 to 20/50 and 1 to 20/70, both eyes requiring myopic lenses. Twenty-two eyes showed no significant change in vision, and 11 eyes showed a loss of vision. Loss of light perception occurred in 8 of the last eyes. Figure 6 shows photographs of 1 of the eyes with a successful result, (a) before the second operation, showing the result of operation 7, and (b) seven months after the second transplantation (operation 152). Clear grafts resulted in 5 eyes, cloudy grafts in 9 eyes and 21 opaque grafts in 21 eyes in this series. The average follow-up period for the group was 46.5 months.

#### COMMENT

The visual and cosmetic results in 165 corneal transplantations have been reviewed in groups arranged according to the diagnosis. Seventeen other transplants were excluded because the results had not been followed for six months after operation. Except for these 17 operations, there has been no exclusion or selection of cases. Many of the unsuccessful results in this series might well be attributed to various preoperative and postoperative complications, but a discussion of this large subject (factors affecting the outcome of the operation) has been deliberately avoided. The sole aim of this survey has been an objective evaluation of the results in an unselected series of corneal transplantations. A discussion of the results in the series as a whole now follows.

*Vision.*—The visual acuities, before and after operation, of the entire series are shown in table 10. The figures between the two heavy lines

running steplike across table 10 represent operations that resulted in no significant change in vision. The figures above the upper heavy line represent operations that resulted in improved visual acuity (better than 20/200). The figures below the lower heavy line represent operations that resulted in a loss of vision. The column of totals on the right side of the table refers to postoperative visual acuity and the row of totals across the bottom refers to preoperative visual acuity.

Preoperative visual acuity was better than 20/200 in 14 eyes, ranged between 20/200 and perception of hand movements in 138 eyes, and was limited to light perception in 13 eyes. Postoperative visual acuity was improved to better than 20/200 in 22 eyes, or 13.3 per cent of the series. There was no significant change in visual acuity in 86 eyes, or 52.1 per cent of the series. A loss of visual acuity followed 57 opera-

TABLE 10.—*Preoperative and Postoperative Visual Acuity in 165 Corneal Transplantations\**

Visual Acuity	Preoperative Visual Acuity									Hand Move- ments	Light Percep- tion	Total No. of Opera- tions
	20/20	20/30	20/40	20/50	20/70	20/100	11-20/ 200	1-10/ 200	Count Fingers			
Postoperative visual acuity												
20/20.....	..	..	..	..	..	..	..	..	..	..	..	..
20/30.....	..	..	..	..	..	..	..	1	3	..	..	4
20/40.....	..	1	..	..	..	..	..	1	..	..	..	2
20/50.....	..	..	..	..	..	..	3	2	..	3	..	8
20/70.....	1	..	..	..	..	..	2	2	1	..	..	6
20/100.....	..	..	..	..	..	..	..	3	..	1	..	4
11-20/200.....	..	..	1	..	1	..	1	3	1	2	..	9
1-10/200.....	..	..	1	..	2	1	2	9	4	1	1	21
Count fingers.....	..	..	..	2	1	1	2	8	14	4	..	32
Hand movements.....	..	..	..	1	..	1	3	8	8	15	3	39
Light perception.....	..	..	..	..	..	..	2	3	6	3	6	20
No light perception.....	..	..	..	..	..	..	..	5	5	7	3	20
Total.....	1	1	2	3	4	3	15	45	42	36	13	165

\* Values above the upper heavy line represent operations which resulted in improvement of vision; figures between the heavy lines, operations which resulted in no change of visual acuity, and values below the lower heavy line, operations which resulted in a loss of visual acuity.

tions, or 34.6 per cent of the series; in 20 of these eyes, or 12.1 per cent of the series, there was loss of light perception. None of the 14 eyes with better than 20/200 preoperative visual acuity obtained any further improvement. In 2 of these eyes visual acuity remained better than 20/200 after operation but was not improved.

A comparison of the visual results in the various diagnostic groups is shown in table 11. Several significant facts are illustrated by this tabulation: Almost half the successful results were obtained in the keratoconus group. In none of the eyes with chemical burns was a successful result attained. Only 2 eyes in the group of 35 eyes with secondary transplantation showed improved vision. Regardless of diagnosis, approximately one third of the operations resulted in decreased

visual acuity. According to the results in this series of operations, successful corneal transplants may be expected in (1) about 30 per cent of eyes with keratoconus; (2) in about 15 per cent of eyes with corneal dystrophy, interstitial keratitis or scarring from trauma; (3) in about 10 per cent of eyes with postinflammatory lesions or scars of unknown origin, and (4) in about 5 per cent of eyes that have already had a previous corneal transplantation.

*Refraction.*—The refractive errors in the 22 eyes with successful visual results are worthy of note. Visual acuity was improved, with correction, to 20/30 in 4 eyes, to 20/40 in 1 eye, to 20/50 in 8 eyes, to 20/70 in 5 eyes and to 20/100 in 4 eyes. To obtain this improvement, 15 eyes required minus lenses and 5 eyes plus lenses, and two

TABLE 11.—*Visual Results of Corneal Transplantation by Diagnostic Groups*

Diagnosis	Number of Operations	Visual Acuity		
		Improved	Unchanged	Decreased
Keratoconus.....	35	10	13	12
Corneal dystrophies.....	13	2	7	4
Interstitial keratitis.....	21	3	11	7
Chemical burns.....	9	..	7	2
Traumatic scars.....	6	1	3	2
Postinflammatory scars.....	22	2	12	8
Scars of unknown cause.....	24	2	11	11
Secondary corneal grafts.....	35	2	22	11
Totals.....	165	22	86	57

eyes showed a mixed astigmatism. The correction in these lenses varied as follows:

	No. of Eyes
Minus sphere with minus cylinder.....	13
Average sphere, 8.4 D	
Average cylinder, 4.3 D	
Minus sphere .....	2
(3.5 and 12.0 D.)	
Plus sphere with plus cylinder .....	3
Average sphere, 3.5 D.	
Average cylinder, 3.0 D.	
Plus sphere (1.0 D.) .....	1
Plus cylinder (2.0 D.) .....	1
Mixed cylinder .....	2
Total .....	22

In addition to the successful results in these 22 eyes, small post-operative increases in visual acuity were obtained in 9 other eyes by means of high minus lenses. Without correction, vision in these eyes varied from perception of hand movements to 5/200, and with correction, from 2/200 to 15/200. The strength of the minus sphere for

these 9 eyes averaged 10.8 D., and the minus cylinders required for the 5 eyes averaged 4.5 D. These facts indicate that the refraction in post-operative corneal transplantation shows a definite trend toward high myopia. Presumably, this is evidence of a tendency in the grafted cornea to bulge.

*Clarity of the Graft.*—There was a marked difference between the number of successful visual results and the number of clear transplants in this series. The cosmetic results were as follows:

	Number	Percentage
Clear transplants.....	44	26.7
Cloudy transplants.....	36	21.8
Opaque transplants.....	81	49.1
Detachment of graft.....	3	1.8
Other (operation 49).....	1	0.6
Total.....	165	

If one were to accept a transparent graft as evidence of a successful operation, as firmly advocated by Thomas,<sup>24</sup> the first two groups of transplantations would be successful. Judged by that standard, 80 operations, or 45.5 per cent of the series, were successful. From a functional point of view, however, this is hardly the case. Of the 44 eyes with clear grafts, visual acuity was improved in 21 eyes, unchanged in 16 eyes and decreased in 7 eyes. Of the 36 eyes with cloudy grafts, visual acuity was improved in 1 eye, unchanged in 27 eyes and decreased in 8 eyes. These results appear to demonstrate rather conclusively that there is no close correlation between transparency of the graft and improvement in vision.

*Follow-up Period.*—The average follow-up for this series of operations was 37.7 months. Patients followed for less than six months were excluded, except those in whom the final result became definite at an earlier date, i. e., detachment of the graft, enucleation or a second corneal transplantation. Omission of these operations would obviously subtract important information from a report. The number of such transplantations, for which the follow-up period was necessarily terminated and the final result known, was considerable (55 operations). Although longer than six months in most instances, the follow-up period was still comparatively short in this group and tended to lower the average for the entire series. When these 55 operations are excluded, the average follow-up period for the remainder of the series becomes 45.7 months. The latter figure, then, is the average follow-up interval for those transplants still under (or potentially under) observation and is more significant in the evaluation of results than the over-all average of 37.7 months.

24. Thomas<sup>8</sup> stated that transparency of the graft or amelioration of the corneal opacity constitutes the criterion for a successful operation.

*Multiple Corneal Transplantations.*—Thus far, the results in this series of corneal transplantations have been discussed only in relation to operations; the visual acuities here tabulated refer to vision in an eye before and after a particular operation, and are not necessarily the initial and/or the final findings for that eye. Approximately one fourth of the eyes undergoing operation in this series later had a second corneal transplantation, and the visual result of the second operation supersedes the result of the initial transplantation. Likewise, the results given up to this point are not applicable on a patient basis, because of the number of secondary operations and because of the number of patients having corneal grafts on both eyes. Clinically, one is more interested in the final result in each eye operated on and in each patient than in the rather abstract results per operation.

In order to analyze the results in this series of operations on the basis of eyes operated on and of patients, the data were rearranged so that all operations on the same eye and/or the same patient were grouped together. The visual results in all patients who had more than one corneal transplantation are shown in table 12. The number of operations falling into this classification was large; of the 165 operations in this series, 96 were performed on 61 eyes of 41 patients who had more than one corneal graft. Part A of table 12 contains the results for 20 patients who had bilateral corneal transplantation, and part B contains the results for 21 patients who had more than one transplantation on one eye. In addition, 13 of the patients in part A had secondary transplantations on one or both eyes. In this multiple operation category, then, 41 patients had 61 initial corneal transplantations and 40 secondary transplantations, making a total of 101 operations for the group. Five of these secondary transplantations were among the 17 operations excluded from evaluation in this series because of a too brief follow-up period. The results in these 5 eyes are not given here except as being unknown, and they are included only because they are necessary to explain the outcome of the initial grafts in these same eyes, which do form part of the series. In the last column in table 12 the final visual acuity for the 61 eyes in the multiple operation group is given; this result is based on comparison of the final visual acuity with the visual acuity before the first corneal transplantation.

Results According to Eyes with Corneal Grafts: The 165 corneal transplantations of this series were performed on 130 eyes of 110 patients, 61 eyes belonging to the 41 patients having multiple operations and the remaining 69 eyes to patients having a single transplantation. The visual results in the 61 eyes of the first group are shown in table 12: improved visual acuity, 13 eyes; no significant change in visual acuity, 17 eyes; decreased visual acuity, 26 eyes, and unknown result, 5 eyes. The visual results in the 69 eyes of patients who had only a single corneal transplantation were not quite so good: improved visual acuity,

TABLE 12.—Visual Results in Cases of Multiple Corneal Transplantations

Case No.	Clinic No.	Eye	Initial Transplant		Secondary Transplant		Totals		Final Visual Acuity *
			Operation No.	Visual Acuity	Operation No.	Visual Acuity	Eye	Patient	
A. Bilateral Transplants									
1.....	509103	OD	1	Improved	...	.....	1	..	Improved
		OS	2	Unchanged	141	Decreased	2	3	Decreased
2.....	560902	OD	4	Unchanged	...	.....	1	..	Unchanged
		OS	7	Decreased	152	Improved	2	3	Improved
3.....	803397	OD	10	Decreased	...	.....	1	..	Decreased
		OS	6	Decreased	159	Improved	2	3	Decreased
4.....	604282	OD	8	Improved	...	.....	1	..	Improved
		OS	9	Decreased	...	.....	1	2	Decreased
5.....	448027	OD	14	Unchanged	...	.....	1	..	Unchanged
		OS	11	Improved	...	.....	1	2	Improved
6.....	729178	OD	17	Improved	...	.....	1	..	Improved
		OS	20	Decreased	...	.....	1	2	Decreased
7.....	745918	OD	18	Improved	...	.....	1	..	Improved
		OS	30	Improved	...	.....	1	2	Improved
8.....	805174	OD	33	Decreased	165	Unchanged	2	..	Decreased
		OS	24	Improved	...	.....	1	3	Improved
9.....	794725	OD	27	Unchanged	Yes, but no follow-up	.....	2	..	(Unknown)
		OS	32	Unchanged	Yes, but no follow-up	.....	2	4	(Unknown)
10.....	497487	OD	53	Unchanged	143	Unchanged	2	..	Unchanged
		OS	52	Unchanged	...	.....	1	3	Unchanged
11.....	489840	OD	54	Improved	...	.....	1	..	Improved
		OS	55	Decreased	149	Unchanged	2	3	Decreased
12.....	633231	OD	58	Unchanged	...	.....	1	..	Unchanged
		OS	60	Unchanged	157	Unchanged	2	3	Unchanged
13.....	766136	OD	62	Improved	...	.....	1	..	Improved
		OS	63	Improved	...	.....	1	2	Improved
14.....	458682	OD	74	Unchanged	147	Unchanged	2	..	Unchanged
		OS	75	Unchanged	134	Unchanged	2	4	Unchanged
15.....	875514	OD	77	Decreased	...	.....	1	..	Decreased
		OS	78	Unchanged	145	Unchanged	..	..	Unchanged
					148	No light perception	3	4	No light perception
16.....	759738	OD	107	Unchanged	...	.....	1	..	Unchanged
		OS	108	Unchanged	133	Decreased	2	3	Decreased
17.....	488464	OD	112	Decreased	...	.....	1	..	Decreased
		OS	110	Unchanged	...	.....	1	2	Unchanged
18.....	509061	OD	113	Unchanged	Yes, but no follow-up	.....	2	..	(Unknown)
		OS	114	Unchanged	Yes, but no follow-up	.....	2	4	(Unknown)
19.....	516335	OD	118	Improved	...	.....	1	..	Improved
		OS	115	Improved	...	.....	1	2	Improved
20.....	557042	OD	127	Decreased	155	Unchanged	2	..	Decreased
		OS	126	Decreased	...	.....	1	3	Decreased
Totals:									
20 patients.....		40	Improved.....12 eyes	Improved.....	2		57 grafts		Improved...13
			Unchanged.....17 eyes	Unchanged.....	8				Unchanged 10
			Decreased.....11 eyes	Decreased.....	3				Decreased...18
				Unknown.....	4				Unknown.... 4
			Total.....40 eyes	Total.....	17				Total.....40
B. Unilateral Transplants									
1.....	644667	OS	13	Unchanged	158	Unchanged	2	..	Unchanged
2.....	813875	OD	26	Decreased	161	No light perception	2	..	No light perception
3.....	561773	OS	40	Decreased	150	Unchanged	2	..	Decreased
4.....	847257	OD	45	Decreased	Yes, but no follow-up	.....	2	..	(Unknown)
5.....	441849	OS	50	Decreased	132	Unchanged	2	..	Decreased
6.....	594229	OD	57	Decreased	154	Unchanged	2	..	Decreased
7.....	610734	OS	59	Decreased	163	Unchanged	2	..	Decreased
8.....	782144	OD	65	Unchanged	162	No light perception	2	..	No light perception
9.....	654802	OD	66	Decreased	164	Unchanged	2	..	Unchanged
10.....	365895	OS	70	Unchanged	131	No light perception	2	..	No light perception
11.....	466643	OD	71	Unchanged	136	Unchanged	..	..	Unchanged
					137	Unchanged	..	..	Unchanged
					140	No light perception	4	..	No light perception
12.....	457018	OD	73	Unchanged	146	Unchanged	2	..	Unchanged
13.....	411857	OD	86	Unchanged	133	Unchanged	2	..	Unchanged
14.....	371425	OS	88	Unchanged	142	Unchanged	2	..	Unchanged
15.....	487454	OS	89	Decreased	139	No light perception	2	..	No light perception
16.....	847335	OD	91	Unchanged	144	No light perception	2	..	No light perception

TABLE 12.—Visual Results in Cases of Multiple Corneal Transplantations—Continued

Case No.	Clinic No.	Eye	Initial Transplant		Secondary Transplant		Totals		Final Visual Acuity *
			Operation No.	Visual Acuity	Operation No.	Visual Acuity	Eye	Patient	
17.....	565344	OD	96	Unchanged	153	Unchanged	2	..	Unchanged
18.....	624147	OD	100	Decreased	156	Unchanged	2	..	Decreased
19.....	439832	OS	109	Unchanged	135	No light perception	2	..	No light perception
20.....	573564	OS	121	Decreased	151	Decreased	2	..	Decreased
21.....	764672	OS	124	Unchanged	160	Unchanged	2	..	Unchanged
Totals									
21 patients.....		21	Improved.....	0	Improved.....	0	44	grafts	Improved.... 0
			Unchanged.....	11	Unchanged.....	14			Unchanged... 7
			Decreased.....	10	Decreased.....	8			Decreased.... 13
			Totals.....	21	Unknown.....	1			Unknown.... 1
					Total.....	23			Total..... 21
Grand Totals (Bilateral and Unilateral Transplants)									
			Visual Acuity		Visual Acuity				
41 patients.....		61	Improved.....	12	Improved.....	2	101	grafts	Improved... 13
		eyes	Unchanged.....	28	Unchanged.....	22	5	(not in	Unchanged... 17
			Decreased.....	21	Decreased.....	11	—	series)	Decreased... 26
			Total.....	61	Unknown†.....	5	96	grafts	Unknown†... 5
					Total.....	40			Total..... 61

\* Not necessarily the same as the visual result of the last operation. This column contains evaluation of the final visual result based on comparison with vision before the first operation. This applies only to patients having secondary corneal transplantations.

† These 5 secondary operations are part of the 17 operations excluded from the series because the patients had not been followed for six months. They are included here to complete the record of multiple operations and to explain the outcome of the first transplantations on these 5 eyes.

8 eyes; no significant change in acuity, 36 eyes, and decreased visual acuity, 25 eyes. A comparison of the results in these two groups is shown in table 13. The fact that the visual results per eye operated on were better in the multiple graft group than in the group having a single transplant suggests that repeated transplantations may yield better results than single operations. Therefore, the visual results in the 130 eyes were surveyed so as to compare the results of single operations with the final outcome of multiple operations. Table 12 contains the data on the 37 eyes that had more than one corneal transplant and on 24 eyes that had a single graft; the latter group was combined with the 69 eyes not in the multiple operation series, making a total of 93 eyes with a single corneal graft. The results of this comparison are also shown in table 13. Only 1 of the 37 eyes that had two or more transplantations showed improved vision; 11 eyes in this group showed no significant change, and 20 eyes had a loss of vision. The results in the 93 eyes that had a single transplantation were better: improved visual acuity, 20 eyes; no significant change in acuity, 42 eyes, and loss of visual acuity, 31 eyes. It is thus evident that, although the results per eye operated on were better in the multiple operation group, the good results were not due to repeated grafts on the same eye. For some undetermined reason, the 20 patients with bilateral transplantations obtained better visual results than the rest of the patients, although 12 of the 13 successful results in this group occurred in eyes with a single transplantation.



*Results on the Basis of Patients.*—In the group of 20 patients who had bilateral corneal transplantations (part A of table 12), 7 patients had 1 graft on each eye, 9 patients had 3 grafts on two eyes; 1 patient had 1 graft on one eye and 3 grafts on the other eye, and 3 patients

TABLE 13.—*Analysis of the Visual Results per Eye with Corneal Graft*

	Number of Eyes	Number of Grafts	Visual Acuity			
			Im- proved	Un- changed	De- creased	Un- known
A. Comparison of Results in Patients Having One Graft with Results in Patients Having Multiple Grafts						
Results per eye in patients with one graft	69	69	8	36	25	..
Results per eye in patients with multiple grafts .....	61	101	13	17	26	5
Totals.....	130	170	21	53	51	5
B. Comparison of Results in Eyes According to Number of Transplantations						
Results in eyes with only one graft.....	93	93	20	42	31	..
Results in eyes with more than one graft	37	77	1	11	20	5
Totals.....	130	170	21	53	51	5

TABLE 14.—*Visual Results in Patients with Bilateral Corneal Transplantation*

Final Visual Result (Visual Acuity)	Patients with One Graft on Each Eye	Patients with Three or More Grafts on Two Eyes	Totals	
Improved				
Improved in both eyes.....	3	..	3	10
Improved in 1 eye and unchanged in other eye	1	1	2	
Improved in 1 eye and decreased in other eye..	2	3	5	
Unchanged				
Unchanged in both eyes.....	..	3	3	3
Decreased				
Unchanged in 1 eye and decreased in other eye	1	1	2	5
Decreased in both eyes.....	..	3	3	
Unknown .....	..	2	2	2
Totals.....	7	13	20	20

had 2 grafts on each eye. The final visual results for these patients with bilateral transplantations are shown in table 14. If improved visual acuity in either one or both eyes is considered a successful result, and a decrease in visual acuity in either eye (unaccompanied with improved visual acuity in the other), a loss of vision, the results in these 20 patients can be classified by the same standards as were the results of the operations and the visual acuity according to eyes, indicated in the preceding sections. Thus, 10 patients obtained improved vision, and

3 showed no significant change in visual acuity. Five patients showed a loss of vision, and the result was unknown in the remaining 2 patients.

The results in the group of 21 patients who had more than 1 corneal transplantation on one eye (part B of table 12) were uniformly poor. None of these patients obtained improvement in vision. There was no significant change in visual acuity in 7 patients, and visual acuity was decreased in 13 patients. The result was unknown in 1 instance. Seven of these patients, or one third of the group, lost all light perception in the eye operated on.

The results in the group of 69 patients who had only 1 transplantation on one eye are obtained from tables 2 to 8; the final visual results were as follows: improved vision, 8 patients; no significant change in visual acuity, 36 patients, and a loss of vision, 25 patients.

The final visual results for the 110 patients, arranged according to the number of transplantations on each eye, are tabulated in table 15.

TABLE 15.—*Visual Results of Corneal Transplantation in 110 Patients*

Number of Operations per Patient	Number of Patients	Final Visual Acuity			
		Im- proved	Un- changed	De- creased	Un- known
One graft on one eye.....	69	8	36	25	..
Two or more grafts on one eye.....	21	..	7	13	1
One graft on each eye.....	7	6	..	1	..
One graft on one eye and two or more on the other eye.....	10	4	2	4	..
Two or more grafts on each eye.....	3	..	1	..	2
Totals.....	110	18	46	43	3

Eighteen patients, or 16 per cent of the series, obtained improvement in vision to better than 20/200 visual acuity in one or both eyes. There was no significant change in vision in 46 patients, or 42 per cent of the series. There was loss of vision, or a decrease in visual acuity in one or both eyes, in 43 patients, or 39 per cent of the series. The final visual result in 3 patients was unknown.

#### CONCLUSIONS

1. There is no accord in the ophthalmologic literature concerning the results of corneal transplantation.

2. Transparency of the graft cannot be considered adequate proof of a successful operation, because clear grafts are frequently seen without any functional improvement in the eye. Normal corneal curvature is as important as clarity of the graft in obtaining a successful optical result.

3. Improvement in vision is the logical index of success in corneal transplantation. Inasmuch as 20/200 visual acuity is commonly accepted as the threshold for industrial blindness, it is suggested that

successful results in corneal transplantation require postoperative improvement in visual acuity to better than 20/200.

4. The visual and cosmetic results of 165 corneal transplantations, performed on 130 eyes of 110 patients, are reviewed:

(a) Visual acuity was improved to better than 20/200 after 22 operations, or 13 per cent of the series. There was no significant change in visual acuity after 86 operations, or 52 per cent of the series. A loss of visual acuity followed 57 operations, or 35 per cent of the series; 20 of these operations, or 12 per cent of the series, were followed by loss of light perception.

(b) Best results were obtained in cases of keratoconus; 10 of the 22 successful operations occurred in the keratoconus group.

(c) Poorest results were obtained in cases with chemical burns of the cornea; none of these operations were successful.

(d) The results of secondary corneal transplants were also poor; only 2 of the 35 operations in this group resulted in improved vision. Eight of these secondary operations resulted in loss of light perception.

(e) Fifteen of the 22 eyes with postoperative improved visual acuity required strong minus lenses to attain this acuity. This postoperative myopia is evidence of a marked tendency of the cornea to bulge after a corneal transplant.

(f) Clear grafts occurred twice as often as improvement in vision in this series of operations.

(g) The average follow-up period for the entire series of operations was 37.7 months.

5. The final visual results in the 130 eyes undergoing corneal transplantation in this series were: improved vision, 21 eyes (16 per cent); no significant change in vision, 53 eyes (41 per cent); loss of vision, 51 eyes (39 per cent), and result unknown, 5 eyes (4 per cent).

(a) Results were better in the eyes with a single transplantation than in the eyes that had multiple grafts.

6. The final visual results on the basis of the 110 patients were as follows: improved vision, 18 cases (16 per cent); no significant change in vision, 46 cases (42 per cent); loss of vision, 43 cases (39 per cent), and unknown result, 3 cases (3 per cent).

(a) Best results were obtained in those patients who had bilateral corneal grafts. Ten of the 20 patients in this group achieved improvement in visual acuity to better than 20/200. Three of these 10 cases obtained successful results in both eyes.

Permission to use the case histories in this report was given by Dr. John H. Dunnington, Director of the Institute of Ophthalmology of the Columbia University-Presbyterian Hospital Medical Center, New York.

704 State Tower Building.

## Correspondence

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### RETROLENTAL FIBROPLASIA

*To the Editor:*—There is, at present, enough confusion on the disease entity “retrolental fibroplasia” in the literature. Unfortunately, in my opinion, this is being further added to by the use of the term “coloboma,” which has appeared in a recent article, in the June 1949 issue of the ARCHIVES.

Paul, in “Blood Groups and Effects of Roentgen Irradiation in Retrolental Fibroplasia,” writes (page 664, case 7): “. . . a falciform fold of the retina in each eye. There was a coloboma of the optic nerve in the left eye.” The author stated that he saw a coloboma. It is quite possible that he did. However, I doubt it, for I have watched several of these enlarged optic disks develop. It is my belief that they occur in the majority of cases of retrolental fibroplasia and that they represent a regular stage of the disease. They can be observed especially in those cases in which development does not progress further than a retinal fold. They can also occasionally be observed in a carefully followed case before the vitreous becomes cloudy or a developing retrolental membrane separating from the ora serrata obscures the details of the fundus.

Briefly, as the fold develops, traction produces blurring of the side of the disk adjacent to this. After a short period (a few days to several weeks, depending on the speed of the disease) a pigmented semicircle begins to appear in the retina on the far side of the disk. This pigmentation is due, I believe, to a localized separation of the retina around the disk resulting from the traction, carrying with it the retinal pigment layer, and is not due to actual pigment. At the edge of this separation, the elevation of the retinal pigment layer almost doubles, so that the area becomes dark. The disk now appears enlarged two, three or four times. The disk and the adjoining retina are elevated from traction. The distribution of the central retinal vessels is still normal. The blood vessels can be followed down into the surrounding retina. Shortly thereafter, further traction distorts the position of the blood vessel on the disk. The outlines of the disk can no longer be identified as such. There remains an enlarged, pale orange to whitish area from which a caput medusa of vessels arises, some vessels going to the retina proper, others running up on the fold.

It is my hope that the term “coloboma” will not enter in the description of retrolental fibroplasia. What has occurred is a post-natal elevation of the disk and surrounding retina, as I have outlined. A coloboma of the disk is a congenital anomaly in which the disk has failed to develop, having a grayish white hole of varying depth and size.

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34½ Beacon Street (8).

## MECHANICS OF INTRACAPSULAR CATARACT EXTRACTION

*To the Editor:*—For the benefit of those who read the paper entitled "Mechanics of Intracapsular Cataract Extraction," by Dr. David O. Harrington, published in the July 1949 issue of the ARCHIVES, I wish to call attention to a slight error. He credits Horner with the introduction of lid sutures in the cataract operation. Evidently he had overlooked my paper read at the meeting of the Chicago Ophthalmological Society in January 1934, and published in the *American Journal of Ophthalmology* in September 1934, from which the following paragraph is quoted:

Upper-lid sutures (fig. 1). Two are used, spaced in the middle of each half of the upper lid. They include the skin only and are placed just above the lash line. The ends are arranged to give an even lift and grasped by a hemostat which is dropped over the top of the head. In many instances this gives all the needed lift and no elevator is required. They permit perfect control in closing the eye after operation and are then fastened to the cheek by adhesive plaster thus holding the temporarily paralyzed lids in apposition. They also afford perfect control at the dressings, as lid lifters, making it unnecessary even to touch the lids.

Speculum. I never use one.

I had used these sutures for many years. The need for them is so obvious that it never occurred to me that their use was original.

RODERIC O'CONNOR, M.D., Oakland, Calif.

411 Thirtieth Street (9).

## News and Notes

EDITED BY DR. W. L. BENEDICT

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### GENERAL NEWS

**Mark J. Schoenberg Memorial Lecture.**—The Mark J. Schoenberg Memorial Lecture was held at the New York Academy of Medicine at 8:30 p. m., Monday, December 5, under the joint sponsorship of the New York Society for Clinical Ophthalmology and the National Society for the Prevention of Blindness. Dr. Jonas S. Friedenwald, of Baltimore, discussed "Problems in the Diagnosis and Treatment of Glaucoma."

This lectureship was established as a memorial to Dr. Schoenberg's interest and original work in the control of glaucoma.

The committee in charge of arrangements for the meeting was composed of Willis S. Knighton, M. D., chairman; Isadore Givner, M.D.; James W. Smith, M.D., and Franklin M. Foote, M.D.

**Nineteenth Annual Midwinter Postgraduate Clinical Convention of the Research Study Club of Los Angeles.**—Among the guest speakers at the nineteenth annual midwinter postgraduate clinical convention of the Research Study Club of Los Angeles, Jan. 16-27, 1950, will be Dr. Conrad Berens and Dr. Raymond Meek, both of New York, and Dr. Meyer Wiener, of Coronado, Calif. In addition, there will be didactic lectures and instruction courses, given largely by representative teachers of the Pacific Coast.

**Research Grants Offered by The National Council to Combat Blindness.**—This organization, which was established for the purpose of financing and stimulating ophthalmologic research, is now offering grants in aid to scientific investigators. Applications to be considered for the first group of awards should be in the office of the Council by Feb. 15, 1950. Application forms may be obtained by addressing the secretary, National Council to Combat Blindness, Inc., 1186 Broadway, New York 1.

**Annual Arthur J. Bedell Lecture.**—Dr. Francis Heed Adler will deliver the annual Arthur J. Bedell Lecture on the evening of March 17, 1950, at the Annual Clinic Conference of the Wills Eye Hospital, Philadelphia.

## SOCIETY NEWS

**Hawaii Eye, Ear, Nose and Throat Society.**—The society held its opening fall meeting at Tripler General Hospital, Honolulu, Territory of Hawaii, on Sept. 15, 1949.

The professional program comprised the following papers: "An Evaluation of Methods of Treatment in 155 Cases of Pterygium," by Lieut. Col. John H. King Jr., with discussions by Drs. Forrest J. Pinkerton, Ogden D. Pinkerton, H. F. Moffat and Philip M. Corboy; and a case report on "Esophageal Stenosis," by Major Aubrey K. Brown, with discussions by Drs. John P. Frazer, L. Q. Pang and Clarence J. Kusunoki.

**Reading Eye, Ear, Nose and Throat Society.**—The Reading Eye, Ear, Nose and Throat Society, Reading, Pa., elected the following officers for the year 1949-1950: president, Dr. William J. Hertz, Allentown; first vice president, Dr. John M. Wotring, Reading; second vice president and president elect, Dr. Roy Deck, Lancaster; treasurer, Dr. Philip R. Wiest, Reading; secretary, Dr. Paul C. Craig, Reading, and program chairman, Dr. C. Fremont Hall, Phoenixville, Pa.

**New Orleans Ophthalmological Society.**—The following officers have been elected: president, Dr. George M. Haik; secretary-treasurer, Dr. N. Leon Hart.

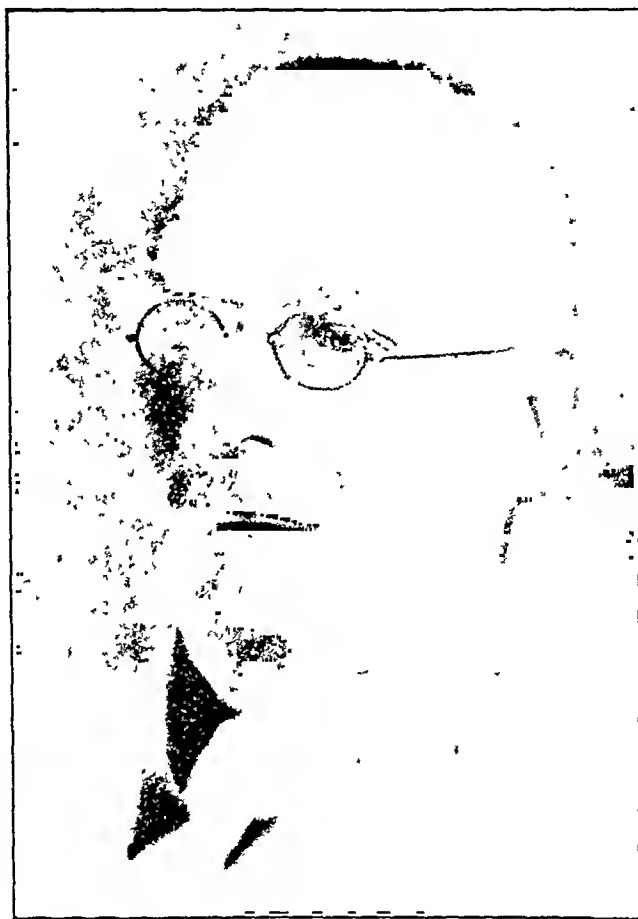
## PERSONAL NEWS

**Prof. Josef Meller's Seventy-Fifth Birthday.**—The occasion of Prof. Josef Meller's seventy-fifth birthday, on October 22, makes this an appropriate time to recognize what he has done for ophthalmology and to speak of many qualities which have made him outstanding. With an inexhaustible capacity for work, he took full advantage of the opportunities offered in Fuchs's clinic in those eventful days of the Vienna school and rapidly advanced, entirely on his own efforts, so that he was ready to carry on in the best tradition of Austrian ophthalmology when the occasion presented itself. As chief of the first ophthalmologic Clinic in Vienna, he proved to be an admirable organizer; he took his profession very seriously, with the persistent aim to uphold its high tradition.

He soon made his mark as a teacher. His unusual command of descriptive language and clarity of expression make him a forceful and interesting speaker. His diction is most comprehensive, with careful regard to grammar and with just the right touch of humor. As a writer he is clear and concise. His many years as one of the editors of the *Zeitschrift für Augenheilkunde* meant many hours of hard work, and he was proud of the admirable way in which he transformed this journal to one of the leaders in the field of ophthalmology; for this reason, the

unhappy way in which his cooperation was brought to a close was particularly distressing.

His investigations have been principally along the line of pathology, and his publications have covered many sides of this important field. As a surgeon, his dexterity was striking, and the soundness of his judgment was as impressive. The many who have profited by his operative courses will never forget the debt he has placed them under. His textbook on ophthalmic operations (*Augenärztliche Eingriffe: Ein Kurzgefasste Operationslehre*, Vienna, Julius Springer, 1946) is the best of



JOSEF MELLER

its kind and cannot be surpassed as an introduction to this difficult art of surgery. It remains an indispensable source of accurate information.

To anticipate the publication of a *Festschrift* at his sixtieth year, he reversed the usual procedure and gathered together some of his publications and speeches in a book entitled "Ausgewählte Schriften und Reden," which he sent to his friends.

A kindly and agreeable personality, he has great charm of manner and grace, and his forthcomingness draws men to him. His culture is wide; he not only is a gifted musician but he keeps up his love of the classics, especially of Horace, whose book of poems has been his constant



and faithful companion through life. He usually passed his spring vacation in Italy, and the summer holidays found him in the beautiful Marienbad region, enjoying the many walks in the pine forests but always ready when the weather turned to rain to study microscopic slides with the aid of his invariably present microscope.

In his partial retirement, let us wish him many years of good health and the maintenance of his interest in the problems of ophthalmology.

# Society Transactions

EDITED BY DR. W. L. BENEDICT

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## OPHTHALMOLOGICAL SOCIETY OF THE UNITED KINGDOM

A. J. Ballantyne, M.D., *President*

James H. Doggart, M.D., and E. F. King, M.B., *Secretaries*

James H. Doggart, M.D., *Reporter*

*Sixty-Seventh Annual Congress, March 27, 28 and 29, 1947*

The Sixty-Seventh Annual Congress of the Ophthalmological Society of the United Kingdom was held in the department of zoology of Glasgow University on March 27, 28 and 29, 1947, under the presidency of Prof. A. J. Ballantyne, LL.D., M.D., F.R.F.P.S., who delivered an address of welcome to the members and guests, especially to those who came from abroad, namely, Dr. P. Mériqot de Treigny (Paris), Prof. W. H. Melanowski (Warsaw), Dr. J. van Canneyt (Ghent), Dr. Erik Godtfredsen (Copenhagen), Madame Suzanne Valons (Paris) and Madame Schiff-Wertheimer (Paris).

### De Senectute. Prof. A. J. Ballantyne.

Under this title, the president delivered an address full of wit and mellow wisdom. He maintained that, although living organisms must sooner or later come to an end, there is good reason to hope that many of the disintegrative processes which now beset us may in time be retarded or modified. The fact that people exhibit such variability in the rate of their decline that even in one and the same body the changes of age so often afflict the separate organs at very different periods and that such discrepancies in the time table can seldom be foretold with accuracy ought to make one realize the complexity of senile change.

Dr. Ballantyne stressed the prevalence of fear among patients with cataract but pointed out that in many instances a simple, encouraging talk by the surgeon is enough to allay such apprehensions. He proceeded to underline the disadvantages of rule of thumb methods in the correction of presbyopia and especially deprecated overcorrection. His closing sentences drew attention to the numerous ways in which older people can continue to give valuable service to the world, but he strongly advocated free scope for the younger generation. Dr. Sinclair's vote of thanks for the address was warmly received by an audience containing many of Dr. Ballantyne's former pupils, who have reason to remember his happy knack of encouraging the young. They know that he, for one, will never lapse into crabbed age and that he will continue to illuminate whatever clinical and pathologic territory may attract his attention in years to come.

### DISCUSSION SESSION

The subject chosen for discussion was, "Rhinology in Relation to Ophthalmology." Dr. J. Marshall, the first opener, pointed out that in dealing with so wide a subject the openers had felt bound to limit the

range of discussion. They had therefore agreed to ignore the controversial question whether, and to what extent, inflamed nasal sinuses might be regarded as a focus of origin of intraocular inflammation or retrobulbar neuritis. Dr. Marshall went on to stress the ophthalmic surgeon's duty of close collaboration with the rhinologist in cases of orbital inflammation, because nasal treatment in many instances offers the best chance of cure. Although he recognized the value of sulfonamide compounds and penicillin, he insisted that these drugs should be used with discrimination, and only after careful review of the clinical signs in each case. Dr. Marshall emphasized the advantages of Dandy's transfrontal approach over the Krönlein operation as a method of exploration for intraorbital neoplasms, because these growths often extend into the cranial cavity. He then referred appreciatively to the work of Dr. Godtfredsen on the ocular symptoms and signs of nasopharyngeal growths. Dacryocystorhinostomy was enthusiastically mentioned by Dr. Marshall, who emphasized that most of the modifications in technic advocated by various operators are of secondary importance. The chief desideratum was the creation of a sufficiently large opening into the nose.

Mr. E. H. Howells, the otorhinolaryngologic surgeon at Moorfields Eye Hospital, was the second opener of the discussion. He gave detailed consideration to the acute and chronic inflammatory disorders of the accessory air sinuses and drew attention to the mechanisms by which infection may spread from one group of cells to another, and thence to the orbit. The direction of proptosis, he suggested, will often provide a clue to which sinus is implicated, but signs may be equivocal. Absence of or trivial symptoms may coexist with severe infection. Aching, when a prominent feature, will often observe a remarkable periodicity, so that some patients can almost set the clock by the onset of neuralgic pain at a regular time of day. Mr. Howells mentioned that the diplopia which follows so large a percentage of operations on the frontal sinus spontaneously subsides in the majority of cases. He also reminded listeners that, although the frontal sinus is rudimentary until the age of 6 years, serious inflammation can arise therein before that age. In dealing with neoplasms, Mr. Howells stressed the advantages of roentgen therapy and the difficulties of surgical intervention. He drew particular attention to the devastating hemorrhage issuing from benign angiofibromas of the nasopharynx if they are touched with a knife. Dacryocystorhinostomy, he said, was not feasible in the management of patients less than 5 years old. Among the nasal conditions interfering with drainage of tears he mentioned hypertrophic rhinitis, lupus and syphilis, as well as trauma resulting from unskilled antrostomy.

Dr. R. McWhirter, representing the roentgenologists, showed a number of excellent pictures illustrating the clinical and roentgenologic features of neoplasms of the accessory sinuses. Diagnosis of such growths is often delayed by their propensity to produce benign polypi as a subsidiary effect. Moreover, these tumors are so rare that the average family physician is unlikely to see more than one or two in the course of thirty years' practice. A common error is to make the diagnosis of disease of the hemopoietic system in young people exhibiting bilateral glandular enlargement in the neck deep to the posterior margin of the sternocleidomastoid muscle, whereas the true diagnosis will

often prove to be a malignant neoplasm of the nasopharynx. He went on to emphasize that so-called nasopharyngeal endothelioma is in reality a carcinoma of the sphenoid sinus, the first manifestation of which may be an ocular palsy. Early stages of this condition respond satisfactorily to roentgen therapy.

During the brief time that remained for discussion at the end of these opening papers, Prof. W. H. Melanowski spoke on orbital cellulitis, which was, in his experience, always due to sinus disease. He also showed pictures to illustrate proptosis resulting from neoplasms of the sinuses and orbit. Dr. Erik Godtfredsen stressed the dangers that beset the orbital contents from the ill directed use of forceps and tamponage in rhinologic operations. He also touched on the differential diagnosis of nasopharyngeal growths and tumors arising in the accessory sinuses. Finally, Mr. B. W. Rycroft claimed benefit from continuous intubation of the nasolacrimal duct in certain cases of deranged tear flow.

#### PAPERS OF THE CONGRESS

##### **Induction of Experimental Tumor of the Lens. PROF. IDA MANN.**

This paper was amply illustrated by pictures of tissue cultures. Having considered the possible reasons that carcinoma of the human lens has never been observed, Professor Mann went on to suggest that nonvascularity would appear to be the most likely explanation. Experimental evidence supports such a theory, for cancer has now been produced in a transplanted lens by controlled tissue culture once the displaced organ has had time to acquire a blood supply. The audience was reminded that all known species share a common organ-specific lens protein. In the course of the subsequent discussion, Professor Mann was congratulated by more than one speaker, and Mr. R. A. Greeves remarked on a similar immunity of the nonvascular cornea to malignant growths.

##### **An Unusual Form of Retinal Detachment (Cystic?) Seen in Children. MR. F. A. JULER.**

The 3 cases described were of children with defective central vision. The retinal detachments were nonprogressive or very slowly progressive and were situated in the lower periphery of one or both retinas. Hemorrhage into the vitreous and large oval rents in the retina were other characteristics. According to Mr. Juler, such cases carry a bad prognosis, and operation is of doubtful value.

Professor Mann agreed with Mr. Juler that cases of this type are not suitable for operation. She maintained that such cysts are in reality intraretinal, so that they are not genuine instances of retinal detachment. Professor Mann also stressed the influence of heredity as an etiologic factor in cysts of the retina.

Mr. C. D. Shapland mentioned a case in which iridocyclitis followed rupture of a retinal cyst. [In this connection, the reporter wishes to remind readers of similar effects produced by the sudden release of crystals, the irritant capacity of which may have remained dormant during long years of enclosure of the crystals within the lens capsule or adventitious intraocular membrane.]

**Epiphora: Diagnosis and Treatment. DR. H. M. TRAQUAIR.**

Nearly every ophthalmic surgeon is interested in epiphora, which has many causes and shows wide individual variations in its response to treatment. With respect to the etiologic significance of intranasal infection, mentioned by several speakers, Dr. Traquair, in his final reply, stated that the nasal condition did not appear to affect his results in the operation of dacryocystorhinostomy so long as he created an adequate opening into the nose.

**Lid and Socket Repair. MR. J. SCOTT TOUGH.**

The author deprecated premature plastic operations and emphasized the importance of hemostasis. He went on to discuss the technic of Z plasty, Imre flaps and Blascovicz rotation flaps. He dwelt on the difficulties of enlarging a contracted socket through plastic surgery and described the value of sustained stretching, rendered possible by splints attached to plaster caps or to the teeth.

**Bilateral Retinal Detachment Associated with Choroidal Cyst.**

DR. J. PENDLETON WHITE AND DR. I. C. MICHAELSON.

The authors invited suggestions concerning treatment for a woman aged 56 whose retina had undergone temporary replacement after a scleral trephination on her only remaining eye. The other eye had been enucleated after development of complicated cataract, and sectioning had revealed general edema of the choroid, together with a large choroidal cyst opposite the globular portion of the retinal detachment. No inflammatory signs had been detected in either eye. Suggestions for treatment made by subsequent speakers included cyclodialysis and the injection of sclerosing fluid.

**Blood Staining of the Cornea. PROF. A. LOEWENSTEIN.**

The author gave an account of 5 cases, in 2 of which the staining was preceded by iridectomy. Of the other 3 instances, in which blood staining arose spontaneously, malignant intraocular growths were present in 2. Professor Lowenstein's paper was illustrated by pictures of microscopic sections. He stressed the importance of a persistent breach of Descemet's endothelium and membrane in the production of blood staining and drew attention to the profound disturbance of corneal metabolism consequent on prolonged imbibition of fluid by the interlamellar spaces of the substantia propria. He reminded his listeners that atropine is contraindicated in such cases.

This paper was discussed by several speakers, including Mr. F. A. Juler, who claimed to have seen blood staining in corneas the endothelium of which was intact. Rupture of deep corneal vessels was mentioned by Mr. J. H. Doggart as a relatively benign form of corneal blood staining. Mr. M. H. Whiting emphasized the desirability of evacuating hyphemas persisting as long as a week, especially after cataract extraction.

**Reiter's Disease: Report of a Case. MR. R. LINDSAY REA.**

In Reiter's original case the picture was that of polyarthritis, urethritis and conjunctivitis, but Mr. Rea's patient, a man aged 29, had bilateral iridocyclitis. The latter complication responded well to heat

and atropine, but a diagnosis of retrobulbar neuritis of the right eye was made five months later, and the condition persisted for three months. Various explanations of Reiter's disease have been put forward, and its origin is uncertain. [The reporter cannot refrain from putting the question: "Is Reiter's disease a clinical entity?"]

**Relation of Sjögren's Disease, the Plummer-Vinson Syndrome (Hypochromic Anemia), and Ariboflavinosis. DR. ERIK GODTFREDSSEN.**

On the basis of a series of 23 patients, all women, with Sjögren's disease, the author concluded that, in spite of many common lesions, especially in epithelial structures, Sjögren's disease is a distinct entity, and not merely a variant of ariboflavinosis or of the Plummer-Vinson syndrome. He stressed the danger of irritant applications to the cornea in cases of Sjögren's disease.

**Holes in the Optic Disk, with Particular Reference to Changes in the Visual Field. MR. HUMPHREY NEAME.**

The author illustrated his report of 9 cases with a number of pictures. Charts of visual fields were shown, and Mr. Neame speculated concerning the mechanism and rationale of the various field defects that may occur in this condition.

**Self-Inflicted Injuries to the Eyes. DR. L. B. SOMERVILLE-LARGE.**

On the basis of his experiences with 360 cases among Indian troops in 1942 to 1945, the author emphasized that, although medical men accustomed to work in India were well acquainted with such lesions, and he himself soon became familiar with them, yet at first he had been mystified by encountering lesions different from anything within his previous experience. He showed pictures of the ocular signs and of the melancholy facial expressions of victims of self-inflicted injury, and he specially mentioned jequirity seeds and fragments of castor oil seeds as the favorite means of producing lesions in the eye. The main clinical features were (a) membranous palpebral conjunctivitis, chiefly of the lower lids; (b) a corresponding lesion of the opposing area of bulbar conjunctiva; (c) enlargement of the ipsilateral preauricular lymph node, and (d) edema of the eyelids. The patients rapidly responded to simple remedies, and symblepharon rarely supervened, except in cases of repeated self infliction of injury. Careful search of the victim's kit usually unearthed a supply of spare seeds.

During the subsequent discussion, Dr. P. Mériqot de Treigny mentioned the ingenious simulation of trachoma on the part of French prisoners deported to work in Germany. These determined opponents of the Reich would produce an alarming crop of follicles by rubbing the upper fornix with an aperient pill, thus insuring repatriation. Dr. H. M. Traquair referred to the employment of aluminum turnings by Continental fanatics endeavoring to produce bloody tears. Mr. R. C. Davenport testified to the occurrence of many cases of similar self-inflicted injuries among Indian troops in France during the First

World War. It should be emphasized that Dr. Somerville-Large's cases all occurred among troops stationed at bases remote from active fighting.

**Vision During Glancing Movements of the Eyes.** DR. G. H. BELL and DR. J. B. DE V. WEIR.

The authors dwelt on the importance of proprioceptive impulses elsewhere in the body as a vital accompaniment of sight. For this reason alone, they contended, the cinema could never supply an utterly satisfactory illusion. To take a simple instance, a screen representation of someone walking up a hill must always remain, so to speak, merely conventional, because no demands are made on the spectator's back and limb muscles. The selective importance of suppression was emphasized, and reference was made to certain experimental difficulties, e. g., the wide variation of response among different subjects, and the difficult task of analyzing phenomena that change every fraction of a second. At any rate, the eye is not a mere camera, and visual images cannot be completely explained in terms of geometry. The cerebral cortex must have its say.

**Concussion Injury to the Eye.** DR. A. M. WRIGHT-THOMSON.

The author analyzed 32 cases encountered during his four years' captivity by the Japanese. He showed a number of pictures and suggested that spasm of the retinal vessels produced by an axon reflex from the choroidal lesion offered the most probable explanation of the clinical signs in such cases. The undoubted existence of traumatic vascular spasm elsewhere in the body was, he said, indirect evidence in support of such an explanation. Changes in tension can easily be interpreted on a similar basis.

**Cysticercus Cellulosae of the Eye.** PROF. W. H. MELANOWSKI.

**Schnabel's Cavernous Atrophy.** MR. EUGENE WOLFF.

This disease, in the author's opinion, is a classic example of the effect of gradual cutting off of blood supply from the optic nerve, producing degeneration of the nerve fibers before that of the supporting connective tissue. Until the glial tissue disappears, which it ultimately does, histologic preparations reveal intact scaffolding, as though the contained nerve fibers had undergone dissolution by a corrosive. Several beautiful illustrations were shown, and Mr. Wolff reminded his listeners that the strength of the lamina cribrosa exhibits considerable variation in individual persons, so that a certain degree of increased tension, persisting for any given time, may easily produce excavation in the disk of one man and leave his neighbor's uncupped.

**Aspects of Disease Affecting the Retinal Veins.** PROF. A. J. BAL-LANTYNE and DR. I. C. MICHAELSON.

The chief conditions mentioned were venous obstruction, Eales's disease and diabetic retinopathy. Although the etiologic factors differ in these three states, and although they typically occur in different age groups, yet the diseases exhibit much in common and may closely resemble each other when far advanced. In all three conditions abnor-

mality of larger veins tends to emerge in the form of sheathing and variation in caliber. Capillary changes are apt to be manifested as hemorrhages, microaneurysms, microexudates and formation of new vessels. Cellular infiltration of the vascular wall is the basis of sheathing in Eales's disease, but anoxemia may produce a similar phenomenon. The stages of diabetic retinopathy were summarized. Dr. Michaelson, who read the paper, gratefully acknowledged the congratulations of Mr. Humphrey Neame and Mr. Eugene Wolff, and went on to mention the joint indebtedness of Dr. Ballantyne and himself to Professor Loewenstein's skill in the histologic preparation of flat sections of the retina.

The paper was amply illustrated.

#### CLINICAL MEETINGS

On the second day of the congress, a clinical meeting was held at the Glasgow Eye Infirmary, under the chairmanship of Dr. Spence Meighan, the president of the Scottish Ophthalmological Club. About 30 cases were presented, representing a number of bizarre results of trauma, together with several rare conditions, such as hypertelorism. An interesting discussion of the cases followed.

#### ANNUAL GENERAL MEETING

Although the routine business of the Society need not be detailed here, the reporter wishes to record that the new treasurer of the Society, Mr. Frank Law, paid tribute to the memory of Sir Arnold Lawson, who died last January, after serving continuously as treasurer for twenty-eight years.

At the close of the Congress, Dr. W. Clark Souter, of Aberdeen, congratulated Dr. Ballantyne on his successful first year of presidency and, after suggesting "*de Amicitia*" as an alternative title for the presidential address, requested that the president should convey the warm greetings of the Society to those friends and colleagues whom he was soon to meet in the United States.

#### SOCIAL EVENTS

Some of the members paid an evening visit to a steel works. On the last afternoon an expedition was made to the Corporation of Glasgow Art Galleries, under the direction of Dr. T. J. Honeyman, a contemporary of the well known playwright James Bridie. Other members and guests visited, by invitation of the University Court, the Hunterian Museum of Glasgow University, which contains a fine collection of Whistler's works, as well as abundant pathologic specimens.

The annual dinner of the Society was held in the Hall of the Royal Faculty of Physicians and Surgeons of Glasgow. Sir Andrew Davidson proposed the health of the Society, and the president responded. The Toast of the Guests was proposed by Dr. Spence Meighan, and Dr. P. Mériqot de Treigny, of Paris, replied in excellent English. Finally, the health of the president of the Society was proposed by Sir Stewart Duke-Elder, who spoke with simple sincerity of the affection and esteem which the mention of Dr. Ballantyne evokes in the hearts of his friends all over the world.



## Book Reviews

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**Blakiston's New Gould Medical Dictionary.** First Edition. Editors: Harold Wellington Jones, M.D.; Normand L. Hoerr, M.D., and Arthur Osol, Ph.D. Pp. 1,294, with 252 illustrations on 45 plates, 129 in color. Price \$10.75. Philadelphia: The Blakiston Company, 1949.

An editorial board and eighty well known contributors present an entirely new medical dictionary to replace the standard "Gould's Medical Dictionary," which has been so popular since its first edition in 1890.

It is difficult to evaluate a dictionary, especially since a reviewer has a bias toward his own specialty and a general medical dictionary is not intended as a reference book in any sense of the word. In spite of this, the present dictionary seems to have kept pace with most developments in the field of ophthalmology and includes items on gonioscopy, anomalous retinal correspondence, epidemic keratoconjunctivitis and many recent developments in the field of ocular therapeutics. Curiously, no mention is made of retrolental fibroplasia, which has general medical interest.

The illustrations are collected in 45 excellent plates, placed conveniently in the middle of the book. Many of these are in color. At the end of the definitions are a number of tables, including compilations of the arteries, veins, bones, joints, muscles, nerves and blood constituents; chemical data on diets, enzymes and hormones; lists of common pathogenic micro-organisms and symbols used in prescription writing. There is even a table of veterinary doses, which is particularly interesting because so many more crude drugs are used for animals than are now in use for man, the list ranging from aconitine to zingiber.

The paper and print are excellent. There is no doubt that this will be received with acclaim by the medical literary world, and the editors, contributors and publishers are to be congratulated on having produced such a beautiful, as well as functional, book.

F. H. ADLER.

**Physiology and Diseases of the Heart and Lungs.** By M. D. Altschule, M.D. Price, \$5. Pp. 368. Cambridge, Mass.: Harvard University Press, 1949.

This book contains no material which would be of direct application to ophthalmology, and yet it should be of interest to all ophthalmologists, especially those engaged in postgraduate teaching, as an excellent example of the application of basic science to clinical medicine. The author's field is cardiology, and he has chosen chronic cardiac decompensation as a clinical entity in which the details of cardiac and circulatory physiology are discussed.

There is an excellent bibliography at the end of each section. It is to be hoped that a similar monograph will appear some day dealing with an ophthalmologic disease entity, such as glaucoma. This book would be an excellent pattern to follow.

FRANCIS H. ADLER.

**Manual for the Objective Examination of the Ocular Muscle Balance.** By Beulah Cushman, M.D. Lithoprinted. Ann. Arbor, Mich.: Edwards Brothers, Inc., 1949.

This is a valuable monograph on methods of examination of the patient with ocular muscle anomalies and the various tests which can be employed to arrive at correct diagnosis. There are brief sections on the value of orthoptics and suggestions for surgical correction. The monograph is well documented with 36 case histories. It can be recommended to all who are interested in strabismus and will be particularly useful for the student preparing for the American Board of Ophthalmology examinations.

FRANCIS H. ADLER.

**Proceedings of the All-India Ophthalmological Society.** Volume IX. Madras Publishing House, Ltd., 1948.

This is a report of the ninth conference of the All-India Ophthalmological Society, held on March 11, 12 and 13, 1948 in Delhi. The conference was to have been held in January, but, owing to the death of Mahatma Ghandi, it was postponed.

FRANCIS H. ADLER.

**The value of Hormones in General Practice.** By W. N. Kemp, M.D. Price, \$3. Pp. 115. Minneapolis: Burgess Publishing Company, 1949.

This monograph is mimeographed and covers in a fairly satisfactory manner recent knowledge concerning the subject of hormones in general practice. Many of the chapters will be of interest to ophthalmologists particularly those dealing with disorders related to the hypothalamus, the pituitary gland and the thyroid. The various pharmaceutical preparations that can be bought on the market are given at the end of each section, together with the specific dosage.

FRANCIS H. ADLER.

**Ocular Signs in Slit-Lamp Microscopy.** By James Hamilton Doggart, M.D. Price, \$6.75. Pp. 112, with 93 illustrations, 85 in color. St. Louis: C. V. Mosby Company, 1949.

This is a short compilation of the changes seen in the anterior segment of the globe with the slit lamp. The colored plates are good, but not comparable to those already published in Vogt, Meesmann, Butler and Berliner's excellent atlases. The chief value of the book is the bibliography. The book is evidently intended to be used as a textbook for the beginner. For this purpose it can be well recommended.

FRANCIS H. ADLER.

**Bulletin and Memoirs of the French Society of Ophthalmology.**  
Paris: Masson & Cie, 1949.

This is a report of the sixty-first meeting of the French Society of Ophthalmology. The session of May 25, 1948 was given over to papers on keratoplasty. In the other four days, a total of fifty-six papers was presented, covering all fields of ophthalmology. These meetings of the French Society of Ophthalmology have been reported in some detail in another issue of the *ARCHIVES*.

FRANCIS H. ADLER.

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## NOTICE

The index for volume 42 will be mailed with the January 1950 number.

